APPENDIX E.1: BACKGROUND INFORMATION ON UNDERSTANDING INFECTIOUS MICROORGANISMS AND THE LANL PROPOSED ACTION MICROORGANISMS

Terminology and Lists of Microorganisms

There are a number of terms used in this document that pertain to infectious microorganisms and these are defined in either footnotes as they are presented in the text or in the glossary at the end of Appendix E.2. These include, biological agents, select agents, etiologic agents, biological warfare agents, and infectious agents. The terminology is often dependant upon the Federal Agency using the term and the Government regulation. For example, "select agent" is a CDC term defined as "a microorganism (virus, bacterium, rickettsia) or toxin…including genetically modified organisms" that can be found in Appendix A of 42 CFR 72. That CFR, however, is titled *Interstate Shipment of Etiologic Agents* and has another table in it (Table 72.3) listing "etiologic agents" as a "viable microorganism or its toxin which causes, or may cause, human disease." There are additional infectious microorganism lists or rankings that are proposed for codification (e.g., 49 FR 171-178).

General Information on Infectious Agents

An instructional guide on infectious diseases that explains many of the terms used in this EA is included as Appendix E.2, and is titled *Understanding Emerging and Re-emerging Infectious Diseases* (NIH 1999). The National Institute of Allergy and Infectious Diseases, one of the National Institutes of Health, prepared the document, which is in the public domain and may be reproduced without permission (NIH 1999). This document was prepared for the NIH Curriculum Supplement Series for Grades 9-12 and includes discussions on:

- The nature of infectious diseases
- Microbes that cause infectious diseases
- The occurrence of infectious disease
- Host defenses against infectious diseases
- Public health measures to prevent infectious diseases
- Treatment of infectious diseases
- Emerging and re-emerging infectious diseases
- Infectious diseases and society
- A glossary of terms

Risk Associated with Infectious Agents

A literature search identified three sources of information ranking infectious agents by risk category. These are from the CDC (CDC 2000a), the NIH (NIH 2001), and a summary compendium that includes an earlier version of the NIH ranking from the American Biological Safety Association (ABSA) (ABSA 1998). The microorganism list from the ABSA summary was used as a starting point for creating the tables in Appendix E.3. The literature search found this listing as the most complete and available from a reliable source. It does not contain all the microorganisms discussed or listed in the CDC BMBL (CDC 1999), nor does the BMBL refer to all the microorganisms listed in the ABSA list. Therefore, those preparing risk assessments should refer to both documents for relevant information. However, as a compendium of possible infectious organisms that might be handled in a microbiological laboratory, it is more than adequate. The tables in Appendix E.3 include some additional microorganisms from the newest CDC (2000a) and NIH (2001) sources. The following subsections briefly describe the three information sources.

CDC 2000 Ranking. The CDC ranking was described in the Johns Hopkins University's *Biodefense Quarterly* (JH 1999), as follows: "On June 3-4, 1999, the Centers for Disease Control and Prevention (CDC) convened a panel of experts in medicine and public health, military intelligence and law enforcement, and security for the purpose of identifying biological agents considered to be of greatest potential concern." The outgrowth of this meeting and subsequent interagency discussion resulted in a CDC *Morbidity and Mortality Weekly Report* (MMWR) that presented the panels recommendations for "critical biological agents" (CDC 2000a). The mandate of this panel was to identify the critical biological agents associated with bioterrorism, the resulting analysis focused on the relative risk between infectious agents that might be of concern.

The CDC segregated the list of agents they deemed most problematic into three categories. Category A included organisms that pose the highest risk. These can be easily disseminated or transmitted person-to-person, cause high mortality (i.e., death) with potential for major public health impact, and require special action for public health preparedness. Category A includes:

- *Variola major* (smallpox)
- *Bacillus anthracis* (anthrax)
- *Yersinia pestis* (plague)
- *Clostridium botulinum* toxin (botulism)
- *Francisella tularensis* (tularaemia)
- filoviruses (Ebola hemorrhagic fever and Marburg fever)
- arenaviruses (Lassa fever, and Junin or Argentine hemorrhagic fever and related viruses)

The second category Category, B, includes microorganisms that are moderately easy to disseminate, have moderate morbidity (i.e., ability to cause disease) and low mortality, but require enhanced disease surveillance. Category B includes:

- *Coxiella burnetti (*Q fever)
- *Brucella spp*. (brucellosis)
- *Burkholderia mallei (*glanders)
- alphaviruses (Venezuelan encephalomyelitis and eastern and western equine encephalomyelitis)
- ricin toxin
- epsilon toxin (from *Clostridium perfringens*)
- *Staphylococcus* enterotoxin B

A subset of Category B includes the food- and water-borne pathogens:

- *Salmonella* species
- *Shigella dysenteriae*
- *Escherichia coli* O 157:H7
- *Vibrio cholerae*
- *Cryptosporidium parvum*

The last and lowest risk category, Category C, includes emerging pathogens that could be engineered for mass dissemination because of availability, ease of production and dissemination, and the potential for high morbidity and mortality and consequent major health impact. These include:

- Nipah virus
- hantaviruses
- tick-borne hemorrhagic fever viruses
- tick-borne encephalitis viruses
- yellow fever
- multi-drug resistant tuberculosis

The NIH 2001 Ranking. The risk group ranking provided by NIH "is based on the potential effect of a biological agent on a healthy human adult and does not account for instances in which an individual may have increased susceptibility to such agents, e.g., pre-existing diseases,

medications, compromised immunity, pregnancy or breast feeding (which may increase exposure of infants to some agents)." This ranking is known as the *Classification of Human Etiologic Agents on the Basis of Hazard* and is included in Appendix B of the *NIH Guidelines: Recombinant DNA and Gene Transfer; Guidelines for Research Involving Recombinant DNA Molecules* (NIH 2001). Agents are classified into four risk groups (RG):

- RG1 includes agents that are not associated with disease in health human adults
- RG2 includes agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are *often* available
- RG3 includes agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions *may* be available
- RG4 includes agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are *not usually* available

The ABSA 1998 Ranking Table. The ABSA "Risk Group Classification for Infectious Agents" (ABSA 1998) was developed on the basis of relative risk. The factors that were taken into consideration were the: pathogenicity of the organism, mode of transmission and host range, availability of effective preventive measures (for example, vaccines), availability of effective treatment (such as antibiotics), and other factors.

The intent of the ranking table is to provide risk information for the research community as part of their biosafety risk assessments. The ABSA tables include four risk-group spreadsheets prepared in Adobe™ portable document format (pdf) that are downloadable from the world-wide-web (http://www.absa.org/riskgroups/). These tables provide information on infectious bacteria, viruses, fungi, and parasites (ABSA 1998). The bacteria table includes Rickettsia, and the virus table includes prions. The ranking information associated with listed microorganisms on these tables reflect the combined sources of information from the European Economic Community directives, the NIH Guidelines on Recombinant DNA, the Canadian Laboratory Biosafety Guidelines, and the CDCs BMBL. These tables are not included in this EA due to their large size.

LANL Proposed Action Microorganisms. LANL envisions that the proposed laboratory facility could handle any of the bacterial or viral infectious agents listed in the BSL-3 category by CDC in Section VII of the BMBL (CDC 1999) or future editions and revisions of that guidance. In addition, the proposed laboratories could handle other bacterial or viral infectious organisms not specifically or currently regulated by CDC or other Federal agencies such as those shown in the tables in Appendix E.3. Only by prior approval of the LANL Institutional Biosafety Committee (IBC), and after a risk analysis is conducted, would any infectious agent be considered for use in the proposed laboratories. Current plans are for these laboratories to handle

live microorganisms or their DNA, RNA[1], proteins[2], or attenuated organisms[3] in their vegetative forms[4] (PC 2001g). The following list provided by LANL (PC 2001g) identifies the bacterial microorganisms and viral diseases that would likely be used in the foreseeable future. (Note: the tables in Appendix E.3 also include these bacterial microorganisms and many of the possible agents that could cause these viral diseases):

- Bacteria
  - Select agents (42 CFR 72)
    - *Bacillus anthracis*
    - *Yersinia pestis*
    - *Burkholderia (Pseudomonas) mallei*
    - *Burkholderia (Pseudomonas) pseudomallei*
    - *Clostridium botulinum*
    - *Francisella tularensis*
    - *Brucella abortus*
    - *Brucella melitensis*
    - *Brucella suis*
    - *Clostridium tetani*
  - *Other bacterial agents listed in the BMBL (CDC 1999)*
    - *Mycobacterium tuberculosis*
    - *Bordetella pertussis*
    - *Helicobacter pylori*
    - *Legionella pneumophilia*
    - *Neisseria gonorrhoeae*
    - *Neisseria meningitidis*
    - *Salmonella typhi*
    - *Shigella spp.*
    - *Vibrionic enteritis*
- Virus
  - *Select agents (42 CFR 72)*
    - *Hantaviruses*
  - *Other viral agents listed in the BMBL (CDC 1999)*
    - *Influenza*
    - *Hepatitis*
    - *Herpesviruses*

[1] RNA or ribonucleic acid is similar and complementary to DNA in that it transcribes the encoded chromosomal information to create proteins. In certain viruses they take the place of DNA.
[2] Proteins are building blocks of cells and are used for support, storage, transport of substances, and defense against invaders.
[3] Organisms that have been deactivated by various means so that they have very limited growth potential.
[4] A vegetative form is one that is capable of actively growing.

- *Poliovirus*
- *Retroviruses*
- *Vesicular stomatitis*
- *Lentiviruses*

There are currently no plans for the proposed BSL-3 laboratories (PC 2001g) to intentionally handle or induce sporulation or the formation of endospores[5], nor are there plans to handle biological toxins except for those produced incidentally to the handling of certain microorganisms.

These microorganisms could be processed a number of ways, for example (PC 2001g):

- Selective culturing[6]
- Sample amplification[7]
- Chemical separation of parts (e.g., DNA, RNA, proteins)
- Centrifugation[8]
- Freezing
- Decontamination by autoclaving[9]
- Decontamination by chemical disinfection

[5] Endospores are a very tough, dormant form of certain bacterial cells that are very resistant to desiccation, heat, and a variety of chemical and radiation treatments that are lethal to vegetative cells.
[6] Selective culturing uses nutrients and environmental controls to enhance the growth of some microorganisms relative to others which might also be present.
[7] Amplification is the process to rapidly and significantly increase the number of microorganisms in a sample.
[8] Centrifugation is the process of spinning a sample at a high rate of revolution to cause a separation of materials based upon their density.
[9] Autoclaving is the process of using steam under pressure for a sufficient time to produce sterilization of materials.

APPENDIX E.2: UNDERSTANDING EMERGING AND RE-EMERGING INFECTIOUS DISEASE

Understanding Emerging and Re-emerging Infectious Diseases

The term "disease" refers to conditions that impair normal tissue function. For example, cystic fibrosis, atherosclerosis, and measles are all considered diseases. However, there are fundamentally different causes for each of these diseases. Cystic fibrosis (CF) is due to a specific genotype that results in impaired transport of chloride ions across cell membranes, leading to the production of abnormally thick mucus. Thus, CF is most accurately called a *genetic* or *metabolic* disease. Atherosclerosis, which can lead to heart attacks and strokes, may be considered a disease of *aging*, because it typically becomes a problem later in life after plaques of cholesterol have built up and partially blocked arteries. In contrast, measles is an *infectious* disease because it occurs when an individual contracts an outside agent, the measles virus. An **infectious disease** is a disease that is caused by the invasion of a host by agents whose activities harm the host's tissues (that is, they cause *disease*) and can be transmitted to other individuals (that is, they are *infectious*).

Nature of Infectious Diseases

Microorganisms that are capable of causing disease are called **pathogens**. Although microorganisms that cause disease often receive the most attention, it is important to note that most microorganisms do *not* cause disease. In fact, many probably provide some protection against harmful microorganisms because they effectively compete with the harmful organisms for resources, preventing them from growing.

A true pathogen is an infectious agent that causes disease in virtually any susceptible host. Opportunistic pathogens are potentially infectious agents that rarely cause disease in individuals with healthy immune systems. Diseases caused by opportunistic pathogens typically are found among groups such as the elderly (whose immune systems are failing), cancer patients receiving chemotherapy (which adversely affects the immune system), or people who have AIDS or are HIV-positive. An important clue to understanding the effect of HIV on the immune system was the observation of a rare type of pneumonia among young men caused by *Pneumocystis carinii*, an organism that causes disease only among the immunosuppressed.

The terms "infection" and "disease" are not synonymous. An **infection** results when a pathogen invades and begins growing within a host. **Disease** results only if and when, as a consequence of the invasion and growth of a pathogen, tissue function is impaired. Our bodies have defense mechanisms to prevent infection and, should those mechanisms fail, to prevent disease after infection occurs. Some infectious agents are easily transmitted (that is, they are very contagious), but they are not very likely to cause disease (that is, they are not very virulent). The polio virus is an example: It probably infects most people who contact it, but only about 5 to 10 percent of those infected actually develop clinical disease. Other infectious agents are very virulent, but not terribly contagious. The terror surrounding Ebola hemorrhagic fever is based on the virulence of the virus (50 to 90 percent fatality rate among those infected); however, the virus itself is not transmitted easily by casual contact. The most worrisome infectious agents are those that are both very contagious and very virulent.

In order to cause disease, pathogens must be able to enter the host body, adhere to specific host cells, invade and colonize host tissues, and inflict damage on those tissues. Entrance to the host typically occurs through natural orifices such as the mouth, eyes, or genital openings, or through wounds that breach the skin barrier to pathogens. Although some pathogens can grow at the initial entry site, most must invade areas of the body where they are not typically found. They do this by attaching to

Figure 3 Emerging and re-emerging infectious diseases threaten all countries. Ebola hemorrhagic fever emerged in African villages; schistosomiasis is re-emerging in Egypt, largely as a consequence of building the Aswan Dam; and legionellosis was identified after an outbreak of pneumonia among individuals attending a conference in Philadelphia.

specific host cells. Some pathogens then multiply between host cells or within body fluids, while others such as viruses and some bacterial species enter the host cells and grow there. Although the growth of pathogens may be enough to cause tissue damage in some cases, damage is usually due to the production of toxins or destructive enzymes by the pathogen. For example, *Corynebacterium diphtheriae*, the bacteria that causes diphtheria, grows only on nasal and throat surfaces. However, the toxin it produces is distributed to other tissues by the circulatory system, damaging heart, liver, and nerve tissues. *Streptococcus pyogenes*, the infectious agent associated with several diseases including strep throat and "flesh-eating disease," produces several enzymes that break down barriers between epithelial cells and remove fibrin clots, helping the bacteria invade tissues.

Microbes That Cause Infectious Diseases

There are five major types of infectious agents: bacteria, viruses, fungi, protozoa, and helminths. In addition, a new class of infectious agents, the prions, has recently been recognized. A brief review of the general characteristics of each of these agents and examples of some diseases they cause follows.

Bacteria. Bacteria are unicellular prokaryotic organisms; that is, they have no organized internal membranous structures such as nuclei, mitochondria, or lysosomes. Their genomes are circular, double-stranded DNA that is associated with much less protein than eukaryotic genomes. Most bacteria reproduce by growing and dividing into two cells in a process known as binary fission. Despite these commonalities that group them together in the Kingdom Monera, there is a wide range of diversity among the bacteria.

There are a variety of morphologies among bacteria, but three of the most common are bacillus (rod-shaped), coccus (spherical), or spirillum (helical rods). The energy sources for bacteria also vary. Some bacteria are photosynthetic and obtain their energy directly from the sun. Others oxidize inorganic compounds to supply their energy needs. Still other bacteria generate energy by breaking down organic compounds such as amino acids and sugars in a respiratory process. Some bacteria require oxygen (aerobes), while others are unable to tolerate it (anaerobes). Some bacteria can grow either with or without oxygen (facultative anaerobes).

Bacteria are frequently divided into two broad classes based on their cell wall structures, which influences their Gram stain reaction. Gram-negative bacteria appear pink after the staining procedure. Familiar pathogenic gram-negative organisms are *Salmonella typhi*, which causes typhoid

fever, and *Yersinia pestis*, which causes plague. Gram-positive bacteria appear purple after the Gram stain procedure. Examples of pathogenic gram-positive bacteria are *Staphylococcus aureus*, which causes skin, respiratory, and wound infections, and *Clostridium tetani*, which produces a toxin that can be lethal for humans.

Viruses. Microbiologists have found viruses that infect all organisms, from plants and animals to fungi and bacteria. Viruses, however, are not organisms themselves because, apart from a host cell, they have no metabolism and cannot reproduce. A virus particle is composed of a viral genome of nucleic acid that is surrounded by a protein coat called a capsid. In addition, many viruses that infect animals are surrounded by an outer lipid envelope, which they acquire from the host cell membrane as they leave the cell. Unlike organisms, in which the genetic material is always double-stranded DNA, viral genomes may be double- or single-stranded DNA (a DNA virus), or double- or single-stranded RNA (an RNA virus).

In the general process of infection and replication by a DNA virus, a viral particle first attaches to a specific host cell via protein receptors on its outer envelope, or capsid. The viral genome is then inserted into the host cell, where it uses host cell enzymes to replicate its DNA, transcribe the DNA to make messenger RNA, and translate the messenger RNA into viral proteins. The replicated DNA and viral proteins are then assembled into complete viral particles, and the new viruses are released from the host cell. In some cases, virus-derived enzymes destroy the host cell membranes, killing the cell and releasing the new virus particles. In other cases, new virus particles exit the cell by a budding process, weakening but not destroying the cell.

In the case of some RNA viruses, the genetic material can be used directly as messenger RNA to produce viral proteins, including a special viral RNA polymerase that copies the RNA template to produce the genetic material for new viral particles. Other RNA viruses, called retroviruses, use a unique enzyme called reverse transcriptase to copy the RNA genome into DNA. This DNA then integrates itself into the host cell genome. These viruses frequently exhibit long latent periods in which their genomes are faithfully copied and distributed to progeny cells each time the cell divides. The human immunodeficiency virus (HIV), which causes AIDS, is a familiar example of a retrovirus.

Just like other infectious agents, viruses cause disease by disrupting normal cell function. They do this in a variety of ways. Some viruses make repressor proteins that stop the synthesis of the host cell's proteins, RNA, and DNA. Viral activity may weaken cell membranes and lysosomal membranes, leading to cell autolysis. Some viral proteins are toxic to cells, and the body's immune defenses also may kill virus-infected cells.

Viruses are classified using a variety of criteria, including shape, size, and type of genome. Among the DNA viruses are the herpes viruses that cause chicken pox, cold sores, and painful genital lesions, and the poxvirus that causes smallpox. Significant RNA viruses that cause human disease include rhinoviruses that cause most common colds; myxoviruses and paramyxoviruses that cause influenza, measles, and mumps; rotaviruses that cause gastroenteritis; and the retroviruses that cause AIDS and several types of cancer.

Fungi. Fungi are eukaryotic, heterotrophic organisms that have rigid cellulose- or chitin-based cell walls and reproduce primarily by forming spores. Most fungi are multicellular, although some, such as yeasts, are unicellular. Together with bacteria, fungi fulfill the indispensable role of decomposers in the environment. Many fungi also infect plants and animals. Examples of diseases caused by fungi are ringworm and histoplasmosis (a mild to severe lung infection transmitted by bat or bird droppings). Yeasts of the *Candida* genus are opportunistic pathogens that may cause diseases such as vaginal yeast infections and thrush (a throat infection) among people who are immunocompromised or undergoing antibiotic therapy. Antibiotics reduce the bacterial population normally present in the throat and vagina, allowing the yeast to grow unchecked.

Protozoa. Protozoa are unicellular, heterotrophic eukaryotes that include the familiar amoeba and

paramecium. Because protozoa do not have cell walls, they are capable of a variety of rapid and flexible movements. Protozoa can be acquired through contaminated food or water or by the bite of an infected arthropod such as a mosquito. Diarrheal disease in the United States can be caused by two common protozoan parasites, *Giardia lamblia* and *Cryptosporidium parvum*. Malaria, a tropical illness that causes 300 million to 500 million cases of disease annually, is caused by several species of the protozoan *Plasmodium*.

Helminths. Helminths are simple, invertebrate animals, some of which are infectious parasites. They are multicellular and have differentiated tissues. Because they are animals, their physiology is similar in some ways to ours. This makes parasitic helminth infections difficult to treat because drugs that kill helminths are frequently very toxic to human cells.

Many helminths have complex reproductive cycles that include multiple stages, many or all of which require a host. *Schistosoma*, a flatworm, causes the mild disease swimmer's itch in the United States; another species of *Schistosoma* causes the much more serious disease schistosomiasis, which is endemic in Africa and Latin America. Schistosome eggs hatch in freshwater, and the resulting larvae infect snails. When the snails shed these larvae, the larvae attach to and penetrate human skin. They feed, grow, and mate in the human bloodstream; the damage to human tissues caused by the accumulating schistosome eggs with their sharp spines results in disease symptoms including diarrhea and abdominal pain. Liver and spleen involvement are common. Another disease due to a helminth is trichinosis, caused by the roundworm *Trichinella spiralis*. This infectious agent is typically ingested in improperly cooked pork from infected pigs. Early disease symptoms include vomiting, diarrhea, and fever; later symptoms include intense muscle pain because the larvae grow and mature in those tissues. Fatal cases often show congestive heart failure and respiratory paralysis.

Prions. During the past two decades, evidence has linked some degenerative disorders of the central nervous system to infectious particles that consist only of protein. These "proteinaceous infectious particles" have been named prions (pree-ons). The known prion diseases include Creutzfeldt-Jakob disease (in humans), scrapie (in sheep), and bovine spongiform encephalopathy ("mad cow disease" in cattle); all known prion diseases frequently result in brain tissue that is riddled with holes. While some prion diseases are inherited, others are apparently due to infection by eating infected tissue or inadvertently through medical procedures such as tissue transplants.

Occurrence of Infectious Diseases

Epidemiology is the study of the occurrence of disease in populations. Epidemiologists are concerned not only with infectious diseases, but also with noninfectious diseases such as cancer and atherosclerosis, and with environmental diseases such as lead poisoning. These professionals work to prevent or minimize the impact of diseases in the population. Their work may include such activities as identifying unusually high incidences of a particular disease, determining the effectiveness of a vaccine, and calculating the cost effectiveness of various means of controlling disease transmission. Occasionally, epidemiologists act as "detectives" who track down the cause of a "new" disease, determine its reservoir and mode of transmission, and help organize various health care workers to bring the disease under control.

Disease reservoirs. The reservoir for a disease is the site where the infectious agent survives. For example, humans are the reservoir for the measles virus because it does not infect other organisms.

Animals often serve as reservoirs for diseases that infect humans. The major reservoir for *Yersinia pestis*, the bacteria that causes plague, is wild rodents. There are also nonliving reservoirs. Soil is the reservoir for many pathogenic fungi as well as some pathogenic bacteria such as *Clostridium tetani*, which causes tetanus.

Modes of transmission. Infectious agents may be transmitted through either direct or indirect contact. Direct contact occurs when an individual is

infected by contact with the reservoir, for example, by touching an infected person, ingesting infected meat, or being bitten by an infected animal or insect. Transmission by direct contact also includes inhaling the infectious agent in droplets emitted by sneezing or coughing and contracting the infectious agent through intimate sexual contact. Some diseases that are transmitted primarily by direct contact with the reservoir include ringworm, AIDS, trichinosis, influenza, rabies, and malaria.

Indirect contact occurs when a pathogen can withstand the environment outside its host for a long period of time before infecting another individual. Inanimate objects that are contaminated by direct contact with the reservoir (for example, a tissue used to wipe the nose of an individual who has a cold or a toy that has been handled by a sick child) may be the indirect contact for a susceptible individual. Ingesting food and beverages contaminated by contact with a disease reservoir is another example of disease transmission by indirect contact. The fecal-oral route of transmission, in which sewage-contaminated water is used for drinking, washing, or preparing foods, is a significant form of indirect transmission, especially for gastrointestinal diseases such as cholera, rotavirus infection, cryptosporidiosis, and giardiasis.

These modes of transmission are all examples of horizontal transmission because the infectious agent is passed from person to person in a group. Some diseases also are transmitted vertically; that is, they are transmitted from parent to child during the processes of reproduction (through sperm or egg cells), fetal development, or birth. Diseases in which vertical transmission occurs include AIDS and herpes encephalitis (which occurs when an infant contracts the herpes simplex type II virus during vaginal birth).

Role of Research in Prevention

Infectious diseases can be prevented at a variety of points, depending on the infectious cycle for the particular disease (Figure 4). Basic research, such as that sponsored by NIH, reveals the specific infectious cycle and details regarding the

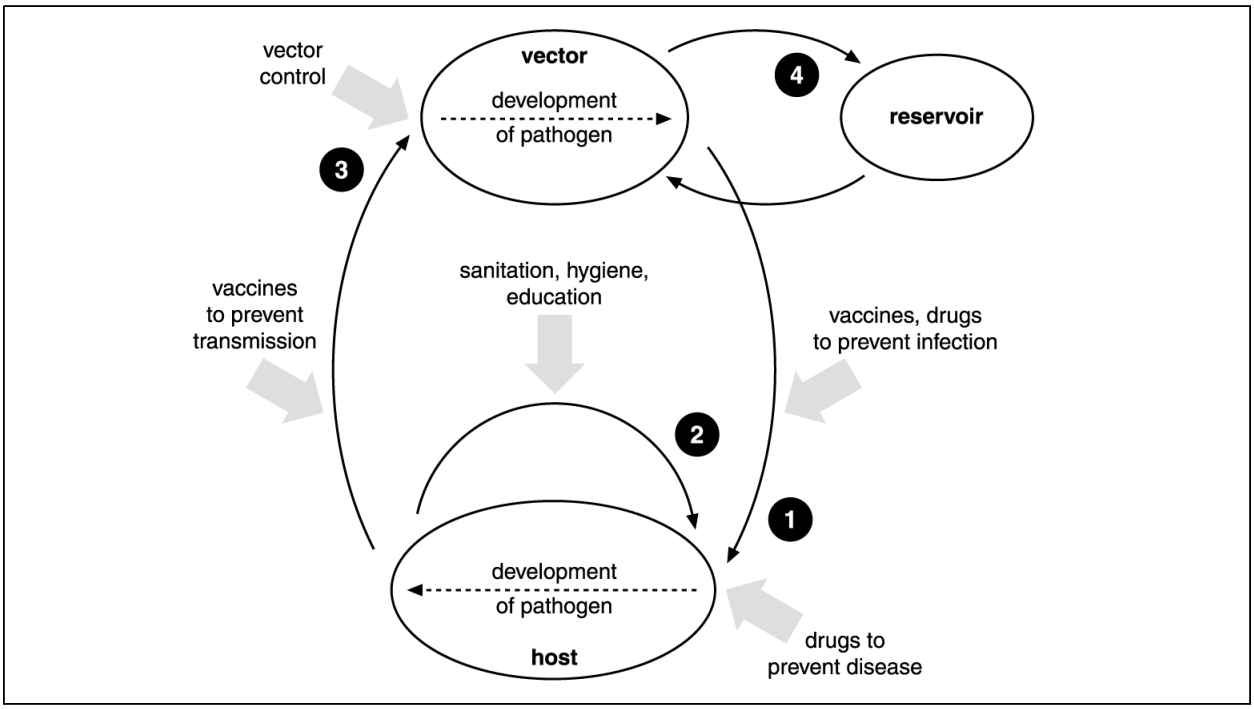


Figure 4 The black arrows illustrate a generalized infectious cycle; the shaded arrows indicate points where infectious diseases can be prevented. (1) A host is infected by the reservoir or a vector for the pathogen. This individual may infect (2) other hosts in a population or (3) new vectors. (4) The pathogen also may cycle between the vector and a reservoir.

activities of the pathogen that cause disease (for example, the particular cells, if any, that are attacked, and the toxins produced by the pathogen that damage host tissues).

Understanding the infectious cycle is critical in order to identify accessible targets for control strategies (Figure 4). For example, direct person-to-person transmission may be inhibited by proper hygiene and sanitary conditions as well as education. Vector-borne diseases may be prevented by control measures that either kill the vector or prevent its contact with humans. Infection by a pathogen or development of a pathogen within a host may be prevented by vaccination. Finally, drugs may be used to prevent infection or suppress the disease process.

In some cases, the tools, including drugs, vaccines and vector control methods, are already available to deal with these diseases. For other diseases, the methods for control are inadequate, undeveloped, or nonexistent. Scientists are trying to develop the new tools needed to banish these scourges of mankind. This requires basic research into the life processes of the pathogen and its interaction with the host in order to identify points within the life cycle where the pathogen is vulnerable to intervention, translational research to develop new tools (such as vaccines or antimicrobial drugs), and clinical research to test the safety and efficacy of these new tools.

Host Defenses Against Infectious Diseases

The human body has several general mechanisms for preventing infectious diseases. Some of these mechanisms are referred to as nonspecific defenses because they operate against a wide range of pathogens. Other mechanisms are referred to as specific defenses because they target particular pathogens and pathogen-infected cells.

Nonspecific mechanisms. Nonspecific mechanisms are the body's primary defense against disease. These mechanisms include anatomical barriers to invading pathogens, physiological deterrents to pathogens, and the presence of normal flora. An example of an anatomical barrier is the nasal opening to the respiratory system. This natural opening is a long, convoluted passage covered by mucous membranes that trap airborne particles and prevent most of them from reaching the lungs. Other anatomical barriers are the skull and vertebral column, which protect the central nervous system—few pathogens are able to penetrate bone. The skin also is a major anatomical barrier to microorganisms. The surface layer of dead, hardened cells is relatively dry, and skin secretions make the surface somewhat acidic. When sweat evaporates, salt is left behind on the skin. All of these conditions (low moisture, low pH, and high salinity) prevent most microorganisms from growing and multiplying on the skin. The major medical challenge in treating burn patients is preventing and treating infections that result because of the absence of skin that ordinarily would prevent invasion of microorganisms.

Natural openings also are protected by a variety of physiological deterrents. For example, tears continually flush debris from the eyes. Vaginal secretions are acidic, a hostile environment that discourages the growth of many pathogens. The eye, mouth, and nasal openings are protected by tears, saliva, or nasal secretions that contain lysozyme, an enzyme that breaks down bacterial cell walls. Blood, sweat, and some tissue fluids contain lysozyme as well.

In addition to lysozyme, the blood has many elements that defend the body from disease-causing organisms. The white blood cells include several types of phagocytic cells that detect, track, engulf, and kill invading bacteria and viruses, as well as infected host cells and other debris. These phagocytic cells are part of the nonspecific immune system. Blood plasma also includes clotting factors that initiate a clot at the injury site, preventing pathogens from invading the body further. Finally, the complement proteins in the blood participate in a cascade of molecular events that result in inflammation, the release of molecules that stimulate phagocytic cells, and the formation of a complex of proteins that binds to the surface of bacterial or infected host cells and lyses those cells.

The inflammatory response is another nonspecific defense mechanism that helps prevent infectious

agents from spreading in the body. Inflammation involves swelling, reddening, elevated temperature, and pain. Unfortunately, inflammation itself frequently causes tissue damage and, in severe cases, even death.

Finally, the protective role of the "normal flora" of microorganisms present on and in the body should not be overlooked. These organisms survive and grow on the skin and in the mouth, gastrointestinal tract, and other areas of the body, but do not cause disease because their growth is kept under control by the host's defense mechanisms and by the presence of other microorganisms. These organisms protect the host by successfully competing with disease-causing organisms, preventing the latter from invading host tissues. When the growth of the normal flora is suppressed (for example, due to antibiotic treatment), other "opportunistic" agents that normally do not grow in or on the body may be able to infect and cause disease.

Specific mechanisms of host resistance. When these nonspecific mechanisms fail, the body initiates a second, specific line of defense. This specific immune response enables the body to target particular pathogens and pathogen-infected cells for destruction. It depends on specialized white blood cells called lymphocytes and includes T-cells (produced from lymphocytes that matured in the thymus gland) and B-cells (produced from lymphocytes that matured in the bone marrow).

The two complementary components of the specific immune response are the cell-mediated response and the antibody-mediated response (Figure 5). The cell-mediated response involves T-cells and is responsible for directly destroying body cells that are infected with a virus or have become cancerous, or for activating other immune cells to be more efficient microbe killers. The antibody-mediated response involves both T-cells and B-cells and is critical for the destruction of invading pathogens as well as the elimination of toxins.

Both the cell-mediated and antibody-mediated responses are initiated after a particular type of phagocytic cell, a macrophage, engulfs a pathogen. Macrophages digest the pathogen and then display antigens from the pathogen on their surface. Antigens are specific molecules, such as the proteins on the surface of pathogens, that elicit an immune response. This display helps the macrophages stimulate specific helper T-cells to release signal molecules called lymphokines. The lymphokines, in turn, stimulate the cell-mediated and antibody-mediated responses.

The cell-mediated response occurs when the lymphokines released from the helper T-cells stimulate other cell types to participate in the immune response. Lymphokine-stimulated killer T-cells attach to the pathogen-infected cells and destroy them, whereas lymphokine-activated phagocytic cells produce more toxic molecules that can kill the pathogen directly.

The antibody-mediated response occurs when the lymphokines activate specific B-cells to produce antibodies (proteins that specifically recognize and bind to antigens). These antibodies attach to antigens on the surface of the pathogens and signal attack by phagocytic cells and complement system. Other B-cells go on to become memory B-cells, which respond quickly by producing more antibodies upon subsequent infection.

Immunity. When a host encounters an antigen that triggers a specific immune response for the second or later time, the memory lymphocytes recognize it and quickly begin growing and dividing, as well as producing high levels of lymphokines and antibodies. Because memory cells are present, this response happens much more quickly than in the initial encounter with the antigen. This rapid response explains why hosts are immune to developing many diseases a second time: The immune response occurs so quickly in a second encounter with the pathogen that the pathogen does not have enough time to reproduce to levels that result in disease before the host's body has destroyed it. The memory response also explains the effectiveness of vaccination for preventing even the first occurrence of many diseases.

Vaccination. A vaccine is either a killed or weakened (attenuated) strain of a particular pathogen, or a solution containing critical antigens from the

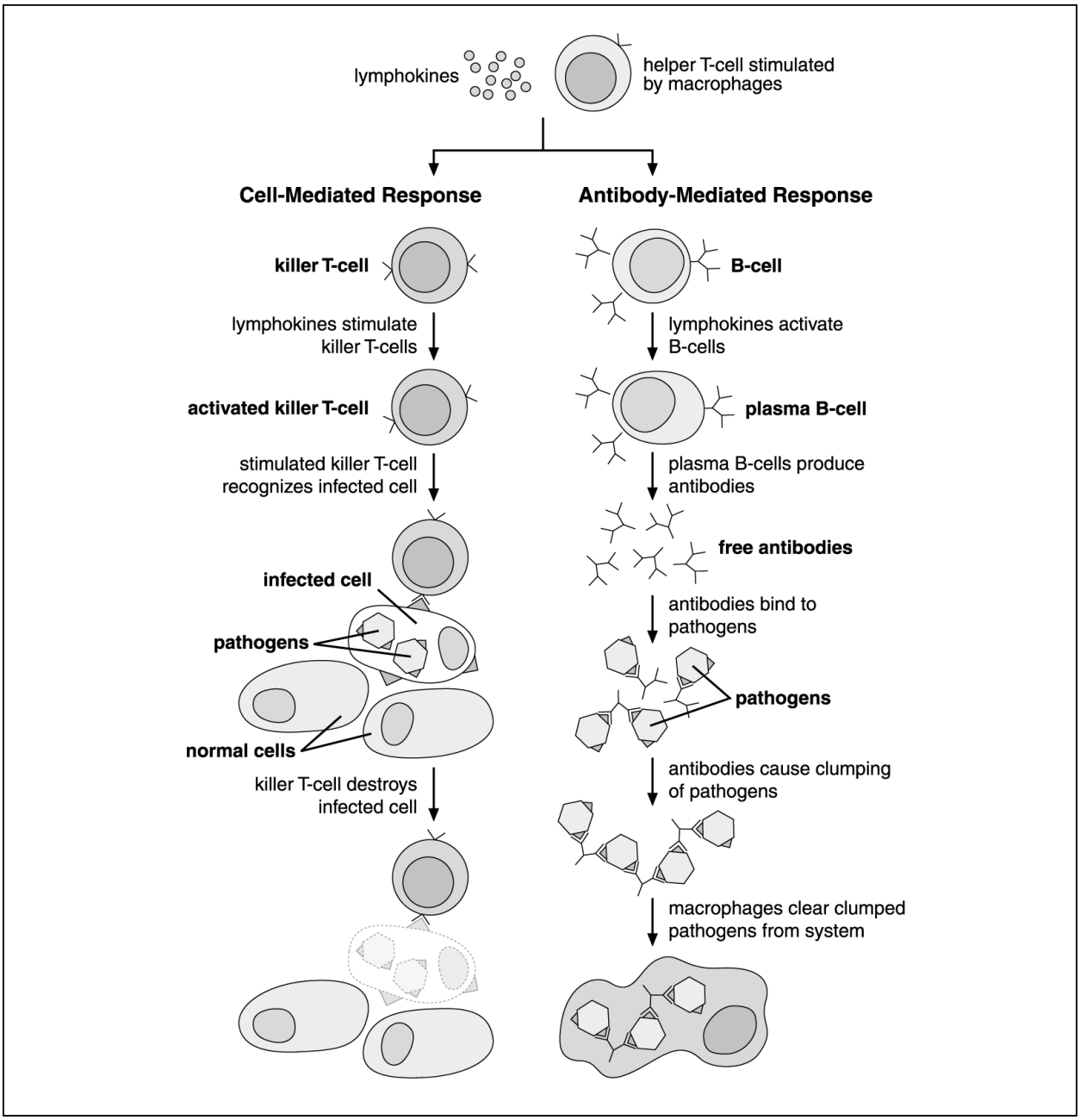


Figure 5 This diagram provides an overview of specific immunity.

pathogen. The body's immune system will respond to these vaccines as if they contain the actual pathogen, even though the vaccine is not capable of causing the disease. As a result of the specific immune response, memory lymphocytes will be present that respond rapidly when the actual pathogen is encountered. The resulting rapid activation of immune cells prevents disease.

Currently new types of vaccines, the DNA vaccines, are in early stage trials. These vaccines contain genes that encode proteins from pathogens. When these genes are inserted into host cells and are expressed in the form of pathogen proteins, an immune reaction may result.

The ultimate effectiveness of vaccination—eradication of the infectious agent—has been achieved only for smallpox. The World Health Organization has identified the polio and measles viruses among the next targets for global eradication.

For a variety of reasons, many diseases are not easily prevented by vaccination. Antibody response is generally the simplest to induce by vaccination, but some pathogens have ways to evade the immune response. Intracellular pathogens (such as viruses and some bacterial and protozoan pathogens) are not directly affected by antibodies because antibodies cannot pass inside cells. Moreover, during the disease process, some pathogens acquire an external coat composed of host-derived material while others disguise themselves by making molecules that resemble host molecules. Thus, the host's immune system does not identify them as foreign invaders. Still other pathogens mutate quickly, producing variants of their antigens that are not recognized by the host's immune system, even though the host survived a previous encounter with that pathogen. Cold and influenza viruses are examples of rapidly mutating pathogens. Scientists are working to improve vaccines against these pathogens.

Public Health Measures to Prevent Infectious Diseases

Developed countries have regulations that help protect the general public from infectious diseases. Public health measures typically involve eliminating the pathogen from its reservoir or from its route of transmission. Those measures include ensuring a safe water supply, effectively managing sewage treatment and disposal, and initiating food safety, animal control, and vaccination programs.

Safe water. Many pathogens that cause gastrointestinal diseases (for example, those that cause cholera and typhoid fever) are transmitted via water. Travelers to developing countries are frequently advised to be immunized against these diseases. This is generally unnecessary in the United States and other developed countries because the water used for washing, drinking, and preparing food is purified before it goes into homes. Purification methods include settling, filtration, and chlorination. The water for homes that use well water or springs is usually safe if guidelines about distance from sewage disposal facilities are followed; however, this water should be checked periodically. When breakdowns in a purification system occur, or when a system is overwhelmed (for example, due to unusual flooding), drinking water may not be safe and should be boiled or treated with chlorine before it is ingested.

Because gastrointestinal pathogens typically leave the body in the feces, public water must be guarded against contamination from sewage. Municipal water is usually tested for the presence of coliform organisms (nonpathogenic microorganisms that are part of the normal flora of the gastrointestinal tract) as indicators of sewage contamination. This procedure is necessary because when the water contains pathogens and is potentially dangerous, the pathogenic organisms are usually present in such small numbers that they are hard to detect.

Sewage treatment and disposal. Sewage includes wash water, water from toilets, and storm run-off. These fluids may carry the pathogens for many waterborne diseases, including giardiasis and hepatitis A; therefore, to ensure public safety the U.S. government (and the governments of other developed countries) requires that sewage be treated to eliminate pathogens. The minimal acceptable level of treatment involves collection and sedimentation of sewage waters, separating solid matter (sludge) from the liquid (effluent) portion of sewage. The effluent is chlorinated to kill pathogens before it is released to rivers or lakes. The sludge is burned or dumped.

More advanced methods of treatment use a secondary treatment following this primary treatment. The effluent is transferred to tanks containing a population of microorganisms that decompose more than 90 percent of the organic wastes and eliminate pathogens by competition (this is another example of the important role of microorganisms in *preventing* disease). The resulting effluent is chlorinated before it is released to the environment. Some sewage treatment plants include a tertiary treatment that involves additional chemicals that also eliminate pathogens.

Food safety programs. The United States has many standards, inspection plans, and regulations about food preparation, handling, and distribution. Meat-packing facilities are inspected regularly to detect and eliminate diseased animals, ensure that standards for processes such as meat cutting and refrigeration are observed, and detect residues from pesticides and antibiotics as well as contamination by bacteria and other parasites. Restaurants and supermarkets are similarly inspected. Milk is pasteurized and dated for sale and is analyzed periodically for contamination. Industry standards for canning and preserving foods are maintained through periodic quality control checks and, if contamination is found in representatives of any batches, public health officials recall the entire batch and alert the public through the media.

Animal control programs. Animals are carriers of many diseases that also affect humans. Inspecting domestic herd animals for tuberculosis (due to the bacterium *Mycobacterium bovis*) and brucellosis (a disease that causes spontaneous abortion in domestic herd animals and abscesses of the liver, spleen, bone marrow, and lymph nodes in humans) has helped eliminate the threat of passing the pathogens for those diseases to humans in contaminated milk and meat. Before their pets can be licensed, dog owners must show proof of rabies vaccination. Because most cases of rabies among people in the United States are due to bites from wild and stray animals, health officials are mandated to impound and destroy these animals. Many diseases, including bubonic plague, are spread by rodents, and rat control, especially in urban areas, is a major component of public health efforts. Insects also transmit many diseases (a notable example is malaria). The spread of insect-borne diseases can be controlled by eliminating breeding areas for insects (for example, draining areas where stagnant water collects) and using pesticides. Many imported animals must be tested for specific diseases to prevent the introduction of those diseases into the country.

Vaccination programs. Most states now require that parents or guardians show proof of vaccination before their children can be enrolled in day-care facilities or public schools, although some states allow certain exemptions, including exemptions based on religious beliefs. The value of immunization for an *individual's health* is obvious; however, it is also important for *public health*. If a certain proportion of a population (called the **threshold proportion**) is immune to a disease, the pathogen that causes that disease will be unable to reproduce itself at a high enough level to maintain itself in the population. This is because once the infected host recovers or dies, there will not be enough new, susceptible hosts for the pathogen to infect. Eventually, the pathogen cannot spread any further and could be eliminated from the population. Even if elimination of the pathogen does not occur, there will be relatively few cases of the related disease and epidemics of the disease in the population will be avoided. This phenomenon is called **herd immunity**.

The threshold proportion varies depending on the disease and other conditions in the relevant population. Vaccination programs led by public health officials aim to achieve the immunization of at least the threshold number of individuals for the population.

Public health organizations. Cities and other local areas have public health agencies that enforce regulations, provide public health services such as vaccination programs, and monitor and report the incidence of particular diseases to state and federal

Figure 6 Vaccination programs are important components of public health systems.

agencies. State public health agencies are affiliated with laboratories and staff epidemiologists for investigating disease cases.

All of these agencies report data to the U.S. Public Health Service. NIH, the funding agency of this module, began in 1887 as the Laboratory of Hygiene; NIH is one of eight health agencies of the U.S. Public Health Service. It supports health-related research aimed at understanding, preventing, treating, and controlling infectious and other diseases of humankind. The Public Health Service also operates the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, and the Food and Drug Administration (FDA). CDC staff investigate disease outbreaks, publish a summary of current epidemiological reports, and sponsor a variety of education programs, research projects, and reference laboratories. FDA monitors the safety of our food, medicines, and many other products that we use daily. Finally, the World Health Organization (WHO) provides international surveillance and control of disease. Among other efforts, WHO coordinates multinational vaccination campaigns.

Treatment of Infectious Diseases

While literally meaning "destroyer of life," the term "antibiotic" has become the most commonly used word to refer to a chemical substance used to treat bacterial infections. The term "antimicrobial" has a somewhat broader connotation, generally referring to anything that inhibits the growth of microbes. Technically, the term antimicrobial does not encompass the "antihelminthic" drugs because worms are not microscopically small. Antimicrobials can be either microbistatic (inhibiting the replication of the microbe) or microbicidal (actually killing the target microorganism). In the former case, a combination of therapy and immunity may be required to finally terminate the infection.

Treatment of bacterial diseases. Because bacteria are prokaryotes, it has been relatively easy to find and develop antibacterial drugs that have minimal side effects. These drugs target structural features and metabolic characteristics of prokaryotes that are significantly different from those in eukaryotic cells. Drugs used to treat bacterial diseases can be grouped into categories based on their modes of action. In general, these drugs inhibit cell wall synthesis, protein synthesis, nucleic acid synthesis, or other enzyme-catalyzed reactions.

The penicillins and cephalosporins all interfere with the synthesis of the peptidoglycan layer in prokaryotic cell walls. Because eukaryotes have neither the peptidoglycan components nor the enzymes that synthesize them, these drugs do not affect the host cells. A second class of drugs, including chloramphenicol, the tetracyclines, and erythromycin, bind to prokaryotic ribosomes and inhibit protein synthesis. Prokaryotic ribosomes are structurally different from eukaryotic ribosomes, so these drugs have minimal effect on eukaryotic cells. Nevertheless, some of them may be toxic to some human tissues when they are used in high doses or for prolonged periods of time.

Rifampicin is one of the antibiotics frequently used for treating tuberculosis. This drug inhibits prokaryotic RNA synthesis. DNA synthesis in prokaryotes may be inhibited by the fluoroquinolones. In contrast, the sulfonamides stop bacterial infections by inhibiting other enzymes. Sulfonamides interfere with the synthesis of folic acid, a vitamin necessary for nucleic acid synthesis. Most bacteria must synthesize their own folic acid because their membranes are impermeable to external folic acid. Mammalian cells are not affected by sulfonamides because they are unable to make their own folic acid and have evolved mechanisms for transporting external folic acid across their membranes.

Treatment of viral diseases. In general, drugs that effectively inhibit viral infections are highly toxic to host cells because viruses use the host's metabolic enzymes in their reproduction. For this reason, most illnesses due to viruses are treated symptomatically until the host's immune system controls and eliminates the pathogen (or the host dies). Antiviral drugs that are used typically target virus-specific enzymes involved in viral nucleic acid synthesis. One of the most familiar of these drugs is acyclovir, which is used to treat outbreaks of genital herpes. Amantadine is an antiviral drug sometimes used to prevent or moderate influenza among those at high risk of severe illness from the disease.

In addition to antiviral drugs that inhibit the replication of the HIV genome (such as AZT), AIDS patients today are also prescribed proteases that interfere with the packaging of the HIV genome into virus particles.

Treatment of fungal and parasitic diseases. The development of drugs to treat fungal, protozoan, and helminthic diseases is challenging because agents that kill or inhibit the growth of these eukaryotic organisms are also highly toxic to mammalian cells. Because fungi and protozoa are rapidly proliferating cells, drugs against these organisms tend to target key components of their replicative or biosynthetic pathways. Common antifungals inhibit sterol syntheses (the azole derivatives) or disrupt the cell membrane (polyenes like amphotericin B). Most antihelminthic drugs target adult worms, which are no longer growing and do not replicate. These drugs are often aimed at inhibiting fundamental processes, such as energy production and muscle function (for example, the benzimidazoles and avermectins), or at targets involved in egg production or larval development.

Malaria, a protozoan disease, was successfully treated for many years with chloroquine. In recent decades, *Plasmodium* species that are resistant to this drug have appeared and spread to areas where malaria is a common threat. In those areas, a combination of the drugs sulfonamide and pyrimethamine is frequently used to treat the disease.

Resistance to antimicrobial agents. One of the ongoing problems scientists and medical workers face in the fight against infectious diseases is the development of resistance to the agents used to control them. The phenomenon of resistance has been known since almost the beginning of antibiotic use. For example, penicillin was introduced for clinical use in treating bacterial infections in the 1940s. As early as 1943, Alexander Fleming, the discoverer of penicillin, observed that some bacteria were resistant to the drug and warned that indiscriminate use of penicillin would lead to the proliferation of resistant pathogenic bacteria. By 1946, medical staff at a London hospital estimated that 14 percent of the staphylococcal strains isolated from their patients were resistant to penicillin. Today, more than 90 percent of these bacteria are resistant. In an environment of widespread penicillin use, selection for resistant bacteria occurred; that is, the pathogenic organisms evolved.

The same process has occurred for many other antimicrobial drugs. Alarmingly, many pathogens are simultaneously acquiring resistance to multiple drugs. For example, some strains of *Mycobacterium tuberculosis* are resistant to all of the currently available drugs used for treatment.

Mechanisms of antimicrobial resistance. Antibiotic resistance appears as a result of changes in genes or the acquisition of genes that allow the pathogen to evade the action of antimicrobial drugs. Resistance mechanisms include structural changes in or around the target molecule that inhibit the drugs' ability to bind to it; reduced permeability of the cell membrane to the drug, actively pumping the drug out of the cell after it has entered; and production of enzymes that inactivate the antibiotic after it has been taken up by the cell. Microbes that produce larger than normal amounts of the target molecule may be "less susceptible" (as opposed to resistant) to a drug, meaning it takes a higher drug level to adversely affect that microbe.

Transfer of antimicrobial-resistance genes. Bacteria have many methods for developing resistance. Antibiotic resistance initially arises as mutations to existing genes; however, many (probably most) bacteria *acquire* these genes rather than experience the mutation themselves. Resistance genes are transferred to other members of the same species and across species by a variety of bacterial genetic exchange mechanisms. Many gram-negative bacteria, including *Escherichia coli* and *Salmonella* species, can transfer extra-chromosomal genetic material called plasmids via the process of *conjugation*. Bacteria endowed with the plasmids have numerous pili along their surfaces; one of these extends to a plasmid-lacking bacterium as a conjugation tube. The plasmid then replicates, and one copy travels through the conjugation tube into the recipient bacterium. One large class of plasmids is called resistance plasmids because they carry genes that confer antibiotic resistance. Many resistance plasmids carry genes for resistance to multiple antibiotics;

thus, one conjugation event can simultaneously transfer resistance to several antibiotics.

Some species of bacteria are capable of taking up free-floating bits of DNA from their environments in a process known as *bacterial transformation*. If they take up a DNA fragment containing an antibiotic resistance gene, they may become resistant to that antibiotic. Another mechanism of genetic exchange in bacteria is *transduction*. Bacteria are subject to viral infection. When a bacteria cell is infected, the virus takes over the cell's metabolism, directing synthesis of its genetic material and production of the components of the viral particle. Simultaneously, the host bacterial DNA is degraded. In the last stage of virus production, its genetic material is encapsulated in a protein coat. Occasionally, a piece of the host bacterial DNA may be packaged in a viral particle. The resulting "transducing particle," like a normal viral particle, has the ability to attach to a recipient bacterium and transfer its genetic material into the cell. However, in this case, the transferred genetic material may be a bacterial gene that provides resistance to an antibiotic.

Finally, many transposons carry antibiotic-resistance genes. Transposons are sequences of DNA that are capable of inserting themselves randomly into genomes. Because they do not appear to rely on specific genetic sequences of the target insertion site, they can readily move across species.

Although mutations that result in antibiotic resistance and, less so, bacterial genetic exchange, are rare events, they need occur only once. In an environment of heavy antibiotic use, the forces of natural selection will favor the propagation of resistant variants of a pathogen. The human body is a rich environment for the growth of large numbers of bacteria and for the interaction of a variety of pathogenic and nonpathogenic bacteria. Thus, there is optimal opportunity for rare mutational and genetic exchange events.

Other pathogens have more limited options for drug resistance. Strains of pathogens develop that are naturally less susceptible to a particular drug due to a normally occurring mutation. In the face of continuing drug use, this strain rapidly grows out of the population being spread through the usual transmission process. Malaria, a protozoan disease, was successfully treated for many years with chloroquine, a drug that was widely available over the counter in regions where malaria was a problem. In recent decades, *Plasmodium* strains that are resistant to this drug have appeared and spread throughout Africa, South America, and Southeast Asia.

Emerging and Re-emerging Infectious Diseases

Fifty years ago many people believed the age-old battle of humans against infectious disease was virtually over, with humankind the winners. The events of the past two decades have shown the foolhardiness of that position. At least a dozen "new" diseases have been identified (such as AIDS, Legionnaire disease, and hantavirus pulmonary syndrome), and traditional diseases that appeared to be "on their way out" (such as malaria and tuberculosis) are resurging. Globally, infectious diseases remain the leading cause of death, and they are the third leading cause of death in the United States. Clearly, the battle has not been won.

Emerging infectious diseases are diseases that (1) have not occurred in humans before (this type of emergence is difficult to establish and is probably rare); (2) have occurred previously but affected only small numbers of people in isolated places (AIDS and Ebola hemorrhagic fever are examples); or (3) have occurred throughout human history but have only recently been recognized as distinct diseases due to an infectious agent (Lyme disease and gastric ulcers are examples). Figure 7 lists several examples of infectious diseases that have emerged in the last three decades.

A review of Figure 7 reveals that environmental changes are related to the emergence of many infectious diseases. For example, Lyme disease, hantavirus pulmonary syndrome (HPS), and Lassa fever all emerged when humans began encountering the insect vector (for Lyme disease) or rodent host (for HPS and Lassa fever) of the causative agents in greater numbers than ever before. Factors related to the emergence of infectious diseases such as Legionnaire disease and hemolytic uremic syndrome include changing

Figure 7 Examples of Emerging Infectious Diseases

Disease	Infectious Agent	Year Recognized*	Contributing Factors
Lassa fever	*Arenaviridae* family (virus)	1969	urbanization and other conditions that favor the rodent host; nosocomial transmission
Ebola hemorrhagic fever	*Filoviridae* family (virus)	1977	unknown natural reservoir; nosocomial transmission
Legionnaire disease	*Legionella pneumophila* (bacterium)	1977	cooling and plumbing systems
hemolytic uremic syndrome	*Escherichia coli* 0157:H7 (bacterium)	1982	mass food production systems
Lyme borreliosis	*Borrelia burgdorferi* (bacterium)	1982	conditions favoring the tick vector and deer, such as reforestation near homes
AIDS	human immunodeficiency virus	1983	migration to cities, global travel, transfusions, organ transplants, intravenous drug use, multiple sexual partners
gastric ulcers	*Helicobacter pylori* (bacterium)	1983	newly recognized as due to infectious agent
cholera	*Vibrio cholerae* 0139 (bacterium)	1992	evolution of new strain of bacteria combining increased virulence and long-term survival in the environment
hantavirus pulmonary syndrome	*Bunyaviridae* family (virus)	1993	environmental changes favoring contact with rodent hosts
pandemic influenza	*Orthomyxoviridae* family (virus)	new viral strains emerge periodically	pig-duck agriculture (possibly)

Sources: Morse, S.S. 1995. Factors in the emergence of infectious diseases. *Emerging Infectious Diseases* [Serial online], 1(1). Available http://www.cdc.gov/ncidod/EID/index.htm. June 1999; Satcher, D. 1995. Emerging infections: Getting ahead of the curve. *Emerging Infectious Diseases* [Serial online], 1(1). Available http://www.cdc.gov/ncidod/EID/index.htm. June 1999; Morse, S.S. (Ed.). 1993. Examining the origins of emerging viruses. *Emerging viruses*. New York: Oxford University Press; ProMED. 1994. About ProMED. Available http://www.fas.org/promed/about/index.html, June 1999.

*Year infectious agent was identified.

technologies: air conditioning systems for the former disease and mass food production for the latter.

Re-emerging infectious diseases are diseases that once were major health problems globally or in a particular country, and then declined dramatically, but are again becoming health problems for a significant proportion of the population (malaria and tuberculosis are examples). Many specialists in infectious diseases include re-emerging diseases as a subcategory of emerging diseases. Figure 8 lists examples of re-emerging infectious diseases.

A review of Figure 8 reveals some explanations for the re-emergence of infectious diseases. Tuberculosis has re-emerged due to evolution of the causative bacteria. The pathogen has acquired resistance to the antibiotics used to treat tuberculosis (either through mutation or genetic exchange) and the long-term use of antibiotics (both within one individual and across the population) has selected for the pathogen's proliferation. Malaria has also become drug resistant, and the vector mosquito has acquired resistance to pesticides as well. The re-emergence of diseases such

Figure 8 Examples of Re-emerging Infectious Diseases

Disease	Infectious Agent	Contributing Factors
cryptosporidiosis	*Cryptosporidium parvum* (protozoa)	inadequate control in water supply; international travel; increased use of child-care facilities
diphtheria	*Corynebacterium diptheriae* (bacterium)	interruption of immunization program due to political changes
malaria	*Plasmodium* species (protozoon)	drug resistance; favorable conditions for mosquito vector
meningitis, necrotizing fasciitis (flesh-eating disease), toxic shock syndrome, and other diseases	Group A *Streptococcus* (bacterium)	uncertain
pertussis (whooping cough)	*Bordetella pertussis* (bacterium)	refusal to vaccinate based on fears the vaccine is not safe; other possible factors: decreased vaccine efficacy or waning immunity among vaccinated adults
rabies	*Rhabdovirus* group (virus)	breakdown in public health measures; changes in land use; travel
rubeola (measles)*	*Morbillivirus* genus (virus)	failure to vaccinate; failure to receive second dose of vaccine
schistosomiasis	*Schistosoma* species (helminth)	dam construction; ecological changes favoring snail host
tuberculosis	*Mycobacterium tuberculosis* (bacterium)	antibiotic-resistant pathogens; immunocompromised populations (malnourished, HIV-infected, poverty-stricken)
yellow fever	*Flavivirus* group (virus)	insecticide resistance; urbanization; civil strife

Sources: Krause, R.M. 1992. The origin of plagues: Old and new. *Science, 257*: 1073-1078; Measles—United States, 1997. April 17, 1998. *Morbidity and Mortality Weekly Report, 47*(14): 273-276; Pertussis vaccination: Use of acellular pertussis vaccines among infants and young children. 1997, March 28. *Morbidity and Mortality Weekly Report, 46*(RR-7); ProMED. 1994. About ProMED. Available from http://www.fas.org/promed/about/index.html. June 1999.

*Following the initial decline of measles cases after the licensing of the vaccine in 1963, there was a resurgence of measles—to some 50,000 cases—from 1989 to 1991. Since then, the incidence of measles has declined again, to an all-time low of 138 cases in 1997.

as diphtheria and whooping cough (pertussis) is related to inadequate vaccination of the population. When the proportion of immune individuals in a population drops below a particular threshold, introduction of the pathogen into the population leads to an outbreak of the disease.

Despite the challenges of emerging and re-emerging infectious diseases, the results of basic research, such as that sponsored by NIH, show that there is reason for hope. AIDS was first described in 1981, and it took two years to identify the retrovirus that causes AIDS, which was named the human immunodeficiency virus. In contrast, less than four months elapsed between the description of hantavirus pulmonary syndrome (HPS) in 1993 and the identification of the previously unknown viral agent, now called Sin Nombre virus. One difference between these two cases is that the years that inter-

vened between the advent of AIDS and the advent of HPS saw the development of polymerase chain reaction, a powerful new research technique that allows rapid identification of causative agents. Recommendations for avoiding and/or treating of new infectious diseases become possible when new techniques, developed through basic research, are applied to the problem of disease emergence.

Other examples of the benefits of basic research include the development of HIV protease inhibitors by researchers funded by NIH and others. These drugs, when used in combination with other anti-HIV drugs, are responsible for the dramatic decrease in deaths from AIDS in the United States. One active area of research at NIH is the development of new types of vaccines based on our new understanding of the immune system. In addition, basic research on the immune system and host pathogen interactions has revealed new points at which vaccines could work to prevent diseases.

Finally, basic research on the ecology of disease organisms—their reservoirs, modes of transmission, and vectors, if any—reveals points at which preventive measures can be used to interrupt this cycle and prevent the spread of disease. For example, research supported by NIAID delineated the mechanism of Lyme disease transmission and how disease results: The tick vector was identified and the life cycle of the causative bacterium was traced through deer and rodent hosts. Understanding this ecology has led to predictions about the regions where and years when the threat of Lyme disease is greatest, as well as recommendations to the public for avoiding infection. These examples and others demonstrate that investment in basic research has great long-term payoffs in the battle against infectious diseases.

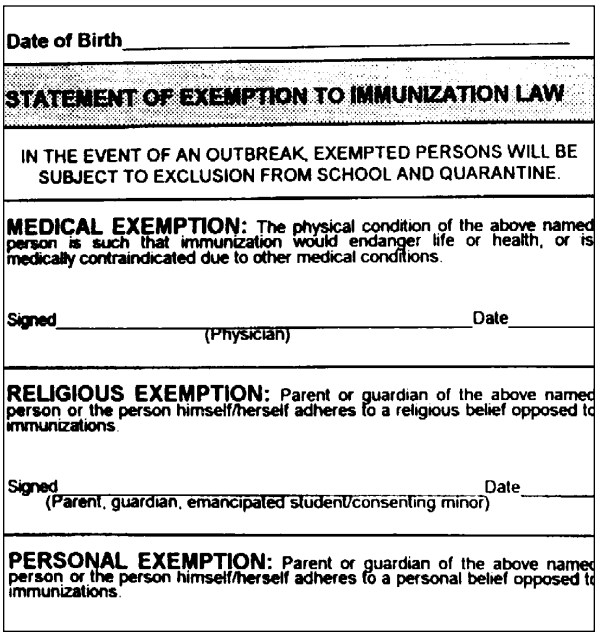
Infectious Diseases and Society

What are the implications of using science to improve personal and public health in a pluralist society? As noted earlier, one of the objectives of this module is to convey to students the relationship between basic biomedical research and the improvement of personal and public health. One way to address this question is by attending to the ethical and public policy issues raised by our understanding and treatment of infectious diseases.

Ethics is the study of good and bad, right and wrong. It has to do with the actions and character of individuals, families, communities, institutions, and societies. During the last two and one-half millennia, Western philosophy has developed a variety of powerful methods and a reliable set of concepts and technical terms for studying and talking about the ethical life. Generally speaking, we apply the terms "right" and "good" to those actions and qualities that foster the interests of individuals, families, communities, institutions, and society. Here, an "interest" refers to a participant's share or participation in a situation. The terms "wrong" or "bad" apply to those actions and qualities that impair interests.

Ethical considerations are complex, multifaceted, and raise many questions. Often, there are competing, well-reasoned answers to questions about what is right and wrong, and good and bad about an individual's or group's conduct or actions. Thus, although science has developed vaccines against many diseases, and public health laws encourage their widespread use, individuals are permitted (in most, but not all, states) to choose not to be vaccinated.

Figure 9 Most states allow exemptions to immunization law.



Date of Birth_____

STATEMENT OF EXEMPTION TO IMMUNIZATION LAW

IN THE EVENT OF AN OUTBREAK, EXEMPTED PERSONS WILL BE SUBJECT TO EXCLUSION FROM SCHOOL AND QUARANTINE.

MEDICAL EXEMPTION: The physical condition of the above named person is such that immunization would endanger life or health, or is medically contraindicated due to other medical conditions.

Signed_____ Date_____
(Physician)

RELIGIOUS EXEMPTION: Parent or guardian of the above named person or the person himself/herself adheres to a religious belief opposed to immunizations.

Signed_____ Date_____
(Parent, guardian, emancipated student/consenting minor)

PERSONAL EXEMPTION: Parent or guardian of the above named person or the person himself/herself adheres to a personal belief opposed to immunizations.

Typically, answers to these questions all involve an appeal to values. A **value** is something that has significance or worth in a given situation. One of the exciting events to witness in any discussion in ethics in a pluralist society is the varying ways in which the individuals involved assign value to things, persons, and states of affairs. Examples of values that students may appeal to in discussions of ethical issues include autonomy, freedom, privacy, protecting another from harm, promoting another's good, justice, fairness, economic stability, relationships, scientific knowledge, and technological progress.

Acknowledging the complex, multifaceted nature of ethical discussions is not to suggest that "anything goes." Experts generally agree on the following features of ethics. First, ethics is a process of rational inquiry. It involves posing clearly formulated questions and seeking well-reasoned answers to those questions. For example, developing countries suffer particularly severely from many infectious diseases because conditions of crowding and poor sanitation are ideal for the growth and spread of pathogens. The same is true for many inner city environments. These places provide a constant reservoir of disease-causing agents. We can ask questions about what constitutes an appropriate ethical standard for allocating health care funds for curtailing the spread of infectious diseases. Should we expend public research dollars to develop drugs whose cost will be out of reach for developing countries or those in the inner cities? Is there any legal and ethical way for the United States to prevent over-the-counter sales of antibiotics in other countries, a practice that may enhance the evolution of antibiotic resistant pathogens? Well-reasoned answers to ethical questions constitute **arguments**. Ethical analysis and argument, then, result from successful ethical inquiry.

Second, ethics requires a solid foundation of information and rigorous interpretation of that information. For example, one must have a solid understanding of infectious disease to discuss the ethics of requiring immunizations and reporting of infectious diseases. Ethics is not strictly a theoretical discipline but is concerned in vital ways with practical matters. This is especially true in a pluralist society.

Third, because tradeoffs among interests are complex, constantly changing, and sometimes uncertain, discussions of ethical questions often lead to very different answers to questions about what is right and wrong and good and bad. For example, we acknowledge that individuals have a right to privacy regarding their infectious disease status. Yet, some argue that AIDS patients who knowingly infect others may have their right to privacy overridden so that partners may be notified of the risk of contracting AIDS.

It is our hope that completing the activities in this module will help students see how understanding science can help individuals and society make reasoned decisions about issues relating to infectious diseases and health. Science provides evidence that can be used to support ways of understanding and treating human disease, illness, deformity, and dysfunction. But the relationships between scientific information and human choices, and between choices and behaviors, are not linear. Human choice allows individuals to choose against sound knowledge, and choice does not necessarily lead to particular actions.

Nevertheless, it is increasingly difficult for most of us to deny the claims of science. We are continually presented with great amounts of relevant scientific and medical knowledge that is publicly accessible. As a consequence, we can think about the relationships among knowledge, choice, behavior, and human welfare in the following ways:

knowledge (what is and is not known) + choice = power

power + behavior = increased human welfare (that is, personal and public health)

One of the goals of this module is to encourage students to think in terms of these relationships, now and as they grow older.

Glossary

acquired immune deficiency syndrome (AIDS): Infectious disease syndrome that is caused by the human immunodeficiency virus (HIV). Characterized by the loss of a normal immune response and increased susceptibility to opportunistic infections and some cancers.

acquired immunity: Specific immunity that develops after exposure to a particular antigen or after antibodies are transferred from one individual to another.

acyclovir: Synthetic drug with antiviral activity against herpes simplex virus. Often used to treat genital herpes.

aerobe: Organism that can grow in the presence of atmospheric oxygen.

airborne transmission: Transmission of an infectious organism in which the organism is truly suspended in the air and travels a meter or more from the source to the host. Chicken pox, flu, measles, and polio are examples of diseases that are caused by airborne agents.

allergen: Substance that can induce an allergic reaction or specific susceptibility.

amantadine: Antiviral compound sometimes used to treat influenza type A infections.

amebiasis: Infection with amoebae. Usually refers to an infection by *Entamoeba histolytica*. Symptoms are highly variable, ranging from an asymptomatic infection to severe dysentery.

amphotericin B: Antibiotic used to treat systemic fungal infections and also used topically to treat candidiasis.

anaerobe: Organism that can grow in the absence of atmospheric oxygen.

anthrax: Infectious disease of animals caused by ingesting the spores of *Bacillus anthracis*. Can occur in humans.

antibiotic: Microbial product, or its derivative, that kills or inhibits the growth of susceptible microorganisms.

antibody: Glycoprotein produced in response to an antigen. Antibodies have the ability to combine with the antigen that stimulated their production.

antibody-mediated immunity: Immunity that results from the presence of antibodies in blood and lymph.

antigen: Foreign (nonself) substance to which lymphocytes respond.

antimicrobial agent: Agent that kills or inhibits the growth of microorganisms.

antiseptic: Chemical applied to tissue to prevent infection by killing or inhibiting the growth of pathogens.

antitoxin: Antibody to a microbial toxin. An antitoxin binds specifically with the toxin, neutralizing it.

arenavirus: Type of RNA virus. Lassa fever is caused by an arenavirus.

autogenous infection: Infection that results from a patient's own microflora.

B-cell: Type of lymphocyte derived from bone marrow stem cells that matures into an immunologically competent cell under the influence of the bone marrow. Following interaction with an antigen, a B-cell becomes a plasma cell, which synthesizes antibodies.

bacillus: Rod-shaped bacterium.

bactericide: Agent that kills bacteria.

binary fission: Asexual reproduction in which a cell separates into two cells.

biologic transmission: Disease transmission in which an infectious organism undergoes some morphologic or physiologic change during its passage through the vector.

botulism: Form of food poisoning caused by a neurotoxin produced by *Clostridium botulinum*. Sometimes found in improperly canned or preserved food.

broad-spectrum drug: Chemotherapeutic agent that is effective across a wide range of different types of pathogens.

candidiasis: Infection caused by a fungus of the genus *Candida*. Typically involves the skin.

carrier: Infected individual who is a potential source of infection for other people.

cell-mediated immunity: Immunity that results from T-cells contacting foreign or infected cells and destroying them.

chemotherapeutic agent: Compound used in the treatment of disease that kills or inhibits the growth of microorganisms and does so at concentrations low enough to avoid doing damage to the host.

chicken pox: Highly contagious skin disease caused by the varicella-zoster virus. Acquired by droplet inhalation into the respiratory system.

cholera: Infectious disease caused by *Vibrio cholerae*.

coccus: Bacterium that is roughly spherical in shape.

common cold: Acute, self-limiting, and highly contagious viral infection of the upper respiratory tract.

communicable disease: Disease associated with an agent that can be transmitted from one host to another.

complement system: Group of circulating plasma proteins that plays a major role in an animal's immune response.

compromised host: Host with lowered resistance to infection and disease for any reason (for example, malnutrition, illness, trauma, or immunosuppression).

conjugation: Form of gene transfer and recombination in bacteria that requires direct cell-to-cell contact.

conjugative plasmid: Plasmid that carries the genes for sex pili and can transfer copies of itself to other bacteria during conjugation.

contact transmission: Transmission of an infectious agent by direct contact of the source or its reservoir with the host.

Creutzfeldt-Jakob disease: Chronic, progressive, fatal disease of the central nervous system caused by a prion.

diphtheria: Acute, highly contagious childhood disease caused by *Corynebacterium diphtheriae*.

disinfectant: Agent that kills, inhibits, or removes microorganisms that may cause disease.

DPT (diphtheria-pertussis-tetanus) vaccine: Vaccine containing three antigens that is used to immunize people against diphtheria, whooping cough, and tetanus.

endemic disease: Disease that is commonly or constantly present in a population, usually at a relatively constant low level.

epidemic: Sudden increase in occurrence of a disease above the normal level in a particular population.

epidemiologist: Person who specializes in epidemiology.

epidemiology: Study of the factors determining and influencing the frequency and distribution of disease, injury, and disability in a population.

eukaryotic cell: Cell that has its genetic material (DNA) enclosed by a nuclear membrane.

facultative anaerobe: Microorganism that does not require atmospheric oxygen, but grows better in its presence.

fungicide: Agent that kills fungi.

genital herpes: Sexually transmitted disease caused by the herpes simplex type II virus.

giardiasis: Intestinal disease caused by the protozoon *Giardia lamblia*.

Gram stain: Differential staining procedure that allows categorization of bacteria into two groups (gram-positive and gram-negative) based on their ability to retain crystal violet when decolorized with an organic solvent such as ethanol.

hantavirus: Type of RNA virus. Hantavirus pulmonary syndrome and Korean hemorrhagic fever are caused by viruses in the genus *Hantavirus*.

harborage transmission: Disease transmission in which an infectious agent does not undergo morphologic or physiologic change during its time inside the vector.

hepatitis A (infectious hepatitis): Type of hepatitis that is transmitted by fecal-oral contamination. It affects mostly children and young adults, especially under conditions of overcrowding and poor sanitation. Caused by the hepatitis A virus.

hepatitis B (serum hepatitis): Type of hepatitis caused by the hepatitis B virus (HBV). Transmitted through body fluids.

herd immunity: Resistance of a population to spread of an infectious organism due to the immunity of a high proportion of the population.

host: Body of an organism that harbors another organism. The host provides a microenvironment that supports the growth and reproduction of the parasitic organism.

human immunodeficiency virus (HIV): Retrovirus that is associated with the onset of AIDS.

immune: Protected against a particular disease by either nonspecific or specific immune defenses.

immune response: Response of the body to contact with an antigen that leads to the formation of antibodies and sensitized lymphocytes. Designed to render harmless the antigen and the pathogen producing it.

immunity: General ability of a host to resist developing a particular disease.

immunology: Science concerned with understanding the immune system and the many factors that are involved with producing both acquired and innate immunity.

index case: First disease case in an epidemic within a population.

infection: Invasion of a host by an agent, with subsequent establishment and multiplication of the agent. An infection may or may not lead to disease.

infectious agent: Living or quasi-living organism or particle that causes an infectious disease. Bacteria, viruses, fungi, protozoa, helminths, and prions are infectious agents.

infectious disease: Change from a state of health to a state in which part or all of a host's body cannot function normally because of the presence of an infectious agent or its products.

inflammation: Localized protective response to tissue injury or destruction. In an acute form, it is characterized by pain, heat, redness, and swelling in the injured area.

influenza (flu): Acute viral infection of the respiratory tract caused by one of three strains of influenza virus (A, B, and C).

intermediate host: Host that serves as a temporary but essential environment for the completion of a parasite's life cycle.

Koch's postulates: Set of rules for proving that a microorganism causes a specific disease.

Koplik's spot: Lesion of the oral cavity caused by the measles virus.

Legionnaire disease: Pulmonary form of disease caused by infection with *Legionella pneumophila*.

Lyme disease: Tick-borne disease caused by the spirochete *Borrelia burgdorferi*.

lymphocyte: Type of white blood cell. Lymphocytes transmit chemical signals that help coordinate the immune system.

malaria: Infectious disease caused by the protozoon *Plasmodium*. Characterized by fever and chills that occur at regular intervals.

measles: Highly contagious skin disease caused by a virus in family *Paramyxoviridae.* The virus enters the body through the respiratory tract or the conjunctiva. Measles is endemic throughout the world.

microbiota (microbial flora): Microorganisms that are normally associated with a particular tissue or organ.

morbidity rate: Number of individuals who become ill with a particular disease within a susceptible population during a specified time period.

mortality rate: Ratio of the number of deaths from a particular disease to the total number of cases of the disease.

nonspecific immunity: General defense mechanisms that provide animals with protection from infection and disease but are not targeted at a particular pathogen.

nosocomial infection: Infection produced by a pathogenic agent that a patient acquires during hospitalization or treatment inside another health care facility.

opportunistic organism: Organism that is usually harmless, but can be pathogenic in a compromised host.

pandemic: Increase in the occurrence of a disease in a large and geographically widespread population. Sometimes called a worldwide epidemic.

parasite: Organism that lives on or within another organism (the host). The relationship benefits the parasite and harms the host.

pasteurization: Process of heating milk and other liquids to destroy microorganisms that can cause spoiling or disease.

pathogen: Disease-producing agent.

pathogenicity: Ability to cause disease.

penicillins: Group of antibiotics that are often used to treat infections by gram-positive bacteria.

peptidoglycan: Large polymer that provides much of the strength and rigidity of bacterial cell walls.

period of infectivity: Time during which the source of an infectious agent is disseminating the agent (is infectious).

plague: Acute, infectious disease with a high mortality rate; caused by *Yersinia pestis.*

plasmid: Circular, double-stranded DNA molecule that can exist and replicate independently of the host cell chromosome or be integrated with it. Although a plasmid is stably inherited, it is not required for bacterial cell growth and reproduction.

poliomyelitis: Acute, contagious viral disease of the central nervous system that can lead to paralysis.

population: Group of organisms of the same species.

prevalence rate: Total number of people infected at one time in a population, regardless of when the disease began.

prion: Infectious particle that is responsible for certain slow-acting diseases such as scrapie in sheep and goats, and Creutzfeldt-Jakob disease in humans. Prions have a protein component, but scientists have not yet detected a nucleic acid component.

prokaryotic cell: Cell that lacks a membrane-delimited nucleus and other membrane-bound organelles. Bacteria are prokaryotic cells.

rabies: Acute infectious disease of the central nervous system caused by an RNA virus of the rhabdovirus group.

reservoir: Site, alternate host, or carrier that harbors pathogenic organisms and serves as a source from which other individuals can be infected.

retrovirus: RNA virus that carries the enzyme reverse transcriptase and forms a DNA copy of its genome during its reproductive cycle.

schistosomiasis: Helminth infection acquired from contact with water containing infected snails.

smallpox: Highly contagious, often fatal disease caused by a poxvirus. Smallpox has been eradicated throughout the world.

source: Location or object from which a pathogen is immediately transmitted to a host.

specific immune response: Collection of several immunological events in which lymphocytes recognize the presence of a particular antigen and act to eliminate it.

spirillum: Rigid, spiral-shaped bacterium.

spirochete: Flexible, spiral-shaped bacterium.

sporadic disease: Disease that occurs occasionally and at random intervals in a population.

superinfection: Bacterial or fungal infection that is resistant to the drug(s) being used to treat it.

T-cell: Lymphocyte derived from bone marrow stem cells that matures into an immunologically competent cell under the influence of the thymus. Involved in cell-mediated immune reactions.

TB skin test: Tuberculin hypersensitivity test to detect a current or past infection with *Mycobacterium tuberculosis.*

tetanus: Often fatal disease caused by the anaerobic, spore-forming bacterium *Clostridium tetani*. Characterized by muscle spasms and convulsions.

toxin: Microbial product or component that at low concentrations can injure a cell or organism.

transduction: Transfer of genes between bacteria by bacteriophages.

transformation: Mode of gene transfer in bacteria in which a piece of DNA in the environment is taken up by a bacterium and integrated into the bacterium's genome.

transposon: DNA segment that carries the genes required for transposition and can move from one place to another in the genome. Often carries genes unrelated to transposition as well.

tuberculosis: Infectious disease resulting from infection by a species of *Mycobacterium*. Infection is usually by inhalation, and the disease usually affects the lungs, although it can occur elsewhere in the body.

vaccination: Administration of a vaccine to stimulate an immune response.

vaccine: Preparation of killed microorganisms; living, weakened (attenuated) microorganisms; inactive or attenuated virus particles; inactivated bacterial toxins; or components (protein, carbohydrate, or nucleic acid) of the microorganism that is administered to stimulate an immune response. Vaccines protect an individual against the pathogenic agent or substance in the future.

vector: Living organism that transfers an infective agent from one host to another.

vector-borne transmission: Transmission of an infectious pathogen between hosts by way of a vector.

virulence: Degree or intensity of pathogenicity of an organism as indicated by mortality rate from the related disease and / or ability to invade tissues and cause disease.

virus: Infectious agent composed of a protein coat and a single type of nucleic acid. Lacks an independent metabolism and reproduces only within a host cell.

whooping cough (pertussis): Infectious disease of the respiratory tract caused by *Bordetella pertussis.*

APPENDIX E.3: BACTERIAL, VIRAL, FUNGAL, AND PARASITE SAFETY CLASSIFICATIONS AND LANL CURRENTLY PROPOSED AND CDC SELECT AGENTS

Table E.3-1. Bacterial Microorganisms and Their Safety Classification

Genus[1]	Species[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Acinetobacter	*spp.*					
Acinetobacter	*baumannii*					2
Acinetobacter	*lwoffi*					
Actinobacillus	*actinomycetem-comiana*					2 implied
Actinobacillus	*spp.*					2
Actinomadura	*madurae*					
Actinomadura	*pelletieri*					
Actinomyces	*bovis*					
Actinomyces	*gerencseriae*					
Actinomyces	*israelii*					
Actinomyces	*naeslundii*					
Actinomyces	*pyogenes*					2
Actinomyces	*spp.*					
Aeromonas	*hydrophilia*					2
Aeromonas	*punctata*					
Aeromonas	*spp.*					
Afpia	*spp.*					
Amycolata	*autotrophica*					2
Arachnia	*propionica*					
Arcanobacterium	*haemolyticum*					2
Archanobacterium	*equi*					
Arizona	*hinshawii*					2
Bacillus	*anthracis*	✸	✸	2/3 (I/E)	A	2
Bacillus	*cereus*					
Bacillus	*subtilis*					1
Bacillus	*licheniformis*					1
Bacillus	*thuringiensis*					
Bacteroides	*fragilis*					
Bacteroides	*spp.*					

[1] Basic genus and specie list is from ABSA 1998 with some additions.
[2] LANL proposed list is from PC 2001b
[3] Select agent list is from 42 CFR 72
[4] Biosafety Level is from CDC 1999 - all organisms shown require import or transfer permit from CDC
[5] Risk Grouping from CDC 2000a
[6] NIH Risk Groups (RG) are from NIH 2001
RG 1 not associated with disease in healthy human adults
RG 2 associated with human disease that is rarely serious and prophylactic intervention ***often*** available
RG 3 associated with human disease that is serious or lethal and prophylactic intervention ***may be*** available
RG 4 associated with human disease that is serious or lethal and prophylactic intervention ***not usually*** available
I/E Requires import and/or export permit from CDC and/or Deparment of Commerce or I/E
AP - animal pathogen
* activities with high droplet or aerosol production potential
✸ applicable organism

Table E.3-1. Bacterial Microorganisms and Their Safety Classification

Genus[1]	Species[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Bartonella	*bacilliformis*					3 implied
Bartonella	*elizabethae*					3 implied
Bartonella	*spp.*					3
Bartonella	*henselae*					2
Bartonella	*quintana*					2
Bartonella	*vinsonii*					2
Bordetella	*spp.*					2
Bordetella	*bronchiseptica*					2 implied
Bordetella	*parapertussis*					2 implied
Bordetella	*pertussis*	✸		2		2
Borrelia	*burgdorferi*					2
Borrelia	*duttoni*					
Borrelia	*recurrentis*					2
Borrelia	*spp.*					
Borrelia	*vincenti*					
Brucella	*abortus*	✸	✸	3 (I/E)	B	3
Brucella	*canis*		✸	3 (I/E)	B	3
Brucella	*melitensis*	✸	✸	3 (I/E)	B	3
Brucella	*ovis*				B	3 implied
Brucella	*spp.* (except *B. ovis*)			3 (I/E)	B	3
Brucella	*suis*	✸	✸	3 (I/E)	B	3
Burkholderia	*spp.*					
Burkholderia	*mallei*	✸	✸	2/3* implied (I/E)	B	3
Burkholderia	*pseudomallei*	✸	✸	2/3* (I/E)		3
Calymmatobacterium	*granulomatis*	✸				
Campylobacter	*coli*	✸		2		2
Campylobacter	*fetus* (*ssp. fetus*)	✸		2		2
Campylobacter	*jejuni*	✸		2		2

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Genus[1]	Species[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Campylobacter	*laridis*	✸				
Campylobacter	*spp.*	✸		2 implied		
Campylobacter	*sputorum*					
Capnocytophaga	*spp.*					
Cardiobacterum	*hominis*					
Chlamydia	*pneumoniae*			2/3*		2
Chlamydia	*psittaci*			2/3*		2
Chlamydia	*spp.* (*C. pneumoniae*)			2/3* implied		3
Chlamydia	*trachomatis*			2/3*		2
Citrobacter	*spp.*					
Clostridium	*botulinum*	✸	✸	2/3*	A	2
Clostridium	*chauvoei*					2
Clostridium	*difficile*					
Clostridium	*equi*					
Clostridium	*haemolyticum*					2
Clostridium	*histolyticum*					2
Clostridium	*novyi*					2
Clostridium	*perfringens*				B	
Clostridium	*septicum*					2
Clostridium	*sordelli*					
Clostridium	*spp.*					
Clostridium	*tetani*	✸		2		2
Corynebacterium	*bovis*					
Corynebacterium	*diphtheriae*			2		2
Corynebacterium	*matruchotii*					
Corynebacterium	*minutissimum*					
Corynebacterium	*pseudotuberculosis*					2
Corynebacterium	*renale*					2
Corynebacterium	*spp.*					

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[4] Biosafety Level is from CDC 1999 - all organisms shown require import or transfer permit from CDC
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Genus[1]	Species[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Corynebacterium	*ulcerans*					
Coxiella	*burnetii*		✸	3 (I/E)	B	3
Dermatophilus	*congolensis*					2
Edwardsiella	*tarda*					2
Eikenella	*corrodens*					
Enterobacter	*aerogenes/cloacae*					
Enterobacter	*spp.*					
Enterococcus	*spp.*					
Erlichia	*sennetsu*					
Erlichia	*spp.*					
Erysipelothrix	*rhusiopathiae*					2
Erysipelothrix	*spp.*					
Escherichia	*coli* (pathogenic strains)			2	B	2
Escherichia	*coli K12* (genetically crippled)					1
Flavobacterium	*meningosepticum*					
Flavobacterium	*spp.*					
Fluoribacter	*bozemanae*					
Francisella	*novocida*					
Francisella	*tularensis* (Type A)		✸	2/3	A	3
Francisella	*tularensis* (Type B)		✸	2/3	A	3
Fusobacterium	*necrophorum*					
Fusobacterium	*spp.*					
Gardnerella	*vaginalis*					
Haemophilus	*ducreyi*					2
Haemophilus	*influenzae*					2
Haemophilus	*spp.*					
Hartmanella	*spp.*					
Helicobacter	*pylori*	✸		2		2
Herellea	*vaginicola*					

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[2] LANL proposed list is from PC 2001b

[3] Select agent list is from 42 CFR 72

[4] Biosafety Level is from CDC 1999 - all organisms shown require import or transfer permit from CDC

[5] Risk Grouping from CDC 2000a

[6] NIH Risk Groups (RG) are from NIH 2001

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Kingella	*kingae*					
Klebsiella	*oxytoca*					1
Klebsiella	*pneumoniae*					2
Klebsiella	*spp.*					2
Lactobacillus	*spp.*					
Legionella	*pneumophila*	✸		2/3*		2
Legionella	*spp.*			2/3*		2
Legionella	*like organisms*			2/3*		
Leptospira	*interrogans*			2 (I/E)		2
Listeria	*ivanovii*			2 implied (I/E)		2 implied
Listeria	*monocytogenes*			2 (I/E)		2 implied
Listeria	*spp.*			2 implied (I/E)		2
Mima	*polymorpha*					
Moraxella	*spp.*					2
Morganella	*morganii*					
Mycobacterium	*africanum*				C	2 implied
Mycobacterium	*asiaticum*			2		2
Mycobacterium	*avium-intracelluare*			2		2
Mycobacterium	*bovis*			2/3 (I/E)	C	3
Mycobacterium	*chelonei*			2		2
Mycobacterium	*fortuitum*			2		2
Mycobacterium	*kansasii*			2		2
Mycobacterium	*leprae*			2		2
Mycobacterium	*malmoense*			2		2
Mycobacterium	*marinum*			2		2
Mycobacterium	*microti*					2 implied
Mycobacterium	*paratuberculosis*			2		2
Mycobacterium	*scrofulaceum*			2		2

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Mycobacterium	*simiae*			2		2
Mycobacterium	*spp.* (except *M. tuberculosis* complex)			2		
Mycobacterium	*szulgai*			2		2
Mycobacterium	*tuberculosis*	✸		3	C	3
Mycobacterium	*ulcerans*			2		2
Mycobacterium	*xenopi*			2		2
Mycoplasma	*hominis*					2 implied
Mycoplasma	*mycoides*					Restricted AP
Mycoplasma	*pneumoniae*					2 implied
Mycoplasma	*agalactiae*					Restricted AP
Mycoplasma	*spp. (except M. mycoides & M. agalactiae)*					2
Neisseria	*gonorrhoeae*	✸		2/3*		2
Neisseria	*meningitidis*	✸		2/3*		2
Neisseria	*spp.*			2/3* implied		
Nocardia	*asteroides*					2
Nocardia	*brasiliensis*					2
Nocardia	*caviae*					
Nocardia	*farcinica*					
Nocardia	*nova*					
Nocardia	*spp.*					
Nocardia	*transvalensis*					2
Nocarida	*otitidis-caviarum*					2
Pasteurella	*haemolytica*					
Pasteurella	*multocida*					3
Pasteurella	*pneumotropica*					
Pasteurella	*spp. (virulent strains)*					3

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Peptostreptococcus	*anaerobius*					
Plesiomonas	*shigelloides*					
Porphyromonas	*spp.*					
Prevotella	*spp.*					
Proteus	*mirabilis*					
Proteus	*penneri*					
Proteus	*spp.*					
Proteus	*vulgaris*					
Providencia	*alcalifaciens*					
Providencia	*rettgeri*					
Providencia	*spp.*					
Pseudomonas	*aeruginosa*					
Pseudomonas	*spp.*					
Rhodococcus	*equi*					2
Rickettsia	*(vole)*					
Rickettsia	*akari*			2/3 (I/E)		3
Rickettsia	*australis*			2/3 (I/E)		3
Rickettsia	*canada*					3
Rickettsia	*conorii*			2/3 (I/E)		3
Rickettsia	*japonicum*			2/3 (I/E)		
Rickettsia	*montana*					
Rickettsia	*mooseri*			2/3 (I/E)		3
Rickettsia	*parkeri*					
Rickettsia	*prowazekii*		✸	2/3 (I/E)		3
Rickettsia	*rhipicephali*					
Rickettsia	*rickettsii*		✸	2/3 (I/E)		3
Rickettsia	*sennetsu*					
Rickettsia	*sibirica*			2/3 (I/E)		3
Rickettsia	*spp.*					

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I/E Requires import and/or export permit from CDC and/or Deparment of Commerce or I/E
AP - animal pathogen
* activities with high droplet or aerosol production potential
✸ applicable organism

Table E.3-1. Bacterial Microorganisms and Their Safety Classification

Genus[1]	Species[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Rickettsia	*tsutsugamushi*			2/3 (I/E)		3
Rickettsia	*typhi (mooseri)*			2/3 (I/E)		3
Salmonella	*arizonae*			2	B	2
Salmonella	*cholerasuis*			2	B	2
Salmonella	*enteritidis*			2	B	2
Salmonella	*gallinarum-pullorum*			2	B	2
Salmonella	*meleagridis*			2	B	2
Salmonella	*paratyphi* (Type A, B, C)			2	B	2
Salmonella	*spp.*			2	B	2 implied
Salmonella	*typhi*	✸		2/3* (I/E)	B	2
Salmonella	*typhimurium*			2	B	2
Serpulina	*spp.*					
Serratia	*marcescens*					
Serretia	*liquefaciens*					
Shigella	*boydii*	✸		2 (I/E) implied		2
Shigella	*dysenteriae* (Type 1)	✸		2 (I/E) implied	B	2
Shigella	*flexneri*	✸		2 (I/E)		2
Shigella	*sonnei*	✸		2 (I/E) implied		2
Shigella	*spp.*	✸		2 (I/E)		2 implied
Sphaerophorus	*necrophorus*					2
Staphylococcus	*aureus*				B	2
Staphylococcus	*epidermidis*				B	
Streptobacillus	*moniliformis*					2
Streptobacillus	*spp.*					
Streptococcus	*agalactiae*					2 implied
Streptococcus	*pneumoniae*					2
Streptococcus	*pyogenes*					2

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Table E.3-1. Bacterial Microorganisms and Their Safety Classification

Genus[1]	Species[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Streptococcus	*spp.*					2
Streptococcus	*suis*					
Treponema	*carateum*					2
Treponema	*pallidum*			2		2
Treponema	*pertenue*					
Treponema	*spp.*					
Treponema	*vincentii*					
Ureaplasma	*urealyticum*					
Vibrio	*cholerae*			2 (I/E)	B	2
Vibrio	*parahaemolyticus*			2 (I/E)		2
Vibrio	*spp.*			2 (I/E) implied		2 implied
Vibrio	*vulnificus*					2
Yersinia	*enterocolitica*					2
Yersinia	*pestis*	✸	✸	2/3* (I/E)	A	3
Yersinia	*pseudotuberculosis*					
Yersinia	*spp.* (except *Y. pestis*)					

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Table E.3-2. Viral Microorganisms and Their Safety Classifications

Viral Group[1]	Name[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Adenoviridae	Adenovirus (human, all types)					2
Arenaviruses	Flexal		*			3
Arenaviruses	Guanarito		*	4 (E)	A	4
Arenaviruses	Junin virus		*	V2 (E), 3/4 (E)	A	V3, 4
Arenaviruses	Lassa fever virus		*	4 (E)	A	4
Arenaviruses	Lymphocytic choriomeningitis (neurotropic virus)			2/3* (E)	A	3
Arenaviruses	Lymphocytic choriomeningitis (non-neurotropic virus)			2/3* (E)		2
Arenaviruses	Machupo virus		*	4 (E)	A	4
Arenaviruses	Mopeia virus (and other Tacaribe viruses)			3		BMBL
Arenaviruses	Sabia		*	4 (E)	A	4
Arenaviruses	Tacaribe complex			2		2
Astroviridae	Astroviridae					
Bunyaviridae	Bunyaviridae (others known to be pathogenic)					
Bunyaviridae/ Bunyavirus Group	Bunyamwera virus			2		2
Bunyaviridae/ Bunyavirus Group	Bunyavirus					
Bunyaviridae/ Bunyavirus Group	California encephalitis virus			2		BMBL
Bunyaviridae/ Bunyavirus Group	Oropouche virus			3		BMBL
Bunyaviridae/ Bunyavirus Group	Tensaw virus			2		BMBL
Bunyaviridae/ Hantaviruses	Black Creek Canal	*	*	2/3 implied (E)	C	3
Bunyaviridae/ Hantaviruses	El Moro Canyon	*	*	2/3 implied (E)	C	3
Bunyaviridae/ Hantaviruses	Hantaan (Korean haemorrhagic fever)	*	*	2/3 (E)	C	3
Bunyaviridae/ Hantaviruses	Hantaviruses (others known)	*	*	2/3* (E)	C	3
Bunyaviridae/ Hantaviruses	Prospect Hill virus	*	*	2/3 implied (E)	C	3
Bunyaviridae/ Hantaviruses	Puumala virus	*	*	2/3 (E)	C	3
Bunyaviridae/ Hantaviruses	Seoul virus	*	*	2/3 (E)	C	3
Bunyaviridae/ Hantaviruses	Sin nombre virus	*	*	2/3 (E)	C	3
Bunyaviridae/ Nairovirus	Nairobi Sheep Disease			3 (I), R		BMBL
Bunyaviridae/ Nairoviruses	Congo Crimean haemorrhagic fever (Tick-borne encephalitis virus)		*	4 (E)	C	4
Bunyaviridae/ Nairoviruses	Hazara virus			2		BMBL
Bunyaviridae/ Phleboviruses	Rift Valley Fever		*	V2 (E), 3 (I/E)		V2, 3
Bunyaviridae/ Phleboviruses	Sandfly fever virus			2		BMBL
Bunyaviridae/ Phleboviruses	Toscana virus			2		BMBL
Bunyaviridae/ Phleboviruses	Zinga (See Rift Valley Fever)			V2 (E), 3 (E)		

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Table E.3-2. Viral Microorganisms and Their Safety Classifications

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Calciviridae	Calciviridae (others known)					2
Calciviridae	Hepatitis E virus	*		2		2
Calciviridae	Norwalk virus					2
Coronaviridae	Coronavirus					2
Filoviridae	Ebola virus		*	4 (E)	A	4
Filoviridae	Marburg virus		*	4 (E)	A	4
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Absettarov (Tick-borne encephalitis virus)		*	3/4 (E)	C	4
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Central European Tick-borne encephalitis virus		*	4 (E)	C	4
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Dengue virus			2		2
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Hanzalova (Tick-borne encephalitis virus)		*	3/4 (E)	C	4
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Hypr (Tick-borne encephalitis virus)		*	3/4 (E)	C	4
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Kokobera			2		BMBL
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Kumlinge (Tick-borne encephalitis virus)		*	3/4 (E)	C	4
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Kunjin			2		BMBL
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Kyasanur Forest (Tick-borne encephalitis virus)		*	4 (E)	C	4
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Looping ill (Tick-borne encephalitis virus)		*	3 (I)	C	BMBL
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Murray Valley encephalitis (Australian encephalitis)			3		BMBL
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Omsk (hemorrhagic fever), (Tick-borne encephalitis virus)		*	4 (E)	C	4
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Powassan			3		BMBL
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Rocio			3		BMBL
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Russian spring-summer encephalitis (Tick-borne encephalitis virus)		*	4 (E)	C	4
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Sammarez Reef			3		BMBL
Flaviviridae/ Flavivirus (Grp B Arbovirus)	St. Louis encephalitis			3		3
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Tick-borne		*		C	BMBL

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Table E.3-2. Viral Microorganisms and Their Safety Classifications

Viral Group[1]	Name[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Wesselsbron virus			3 (I)		BMBL
Flaviviridae/ Flavivirus (Grp B Arbovirus)	West Nile fever virus			3 (E)		BMBL
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Yellow fever virus (vaccine strain 17D)			V2 (E)		2
Flaviviridae/ Flavivirus (Grp B Arbovirus)	Yellow fever virus (wild type)		*	3 (E)	C	3
Flaviviridae/Flavivirus (Grp B Arbovirus)	Japanese B encephalitis			3 (E)		3
Flaviviridae/Flavivirus (Grp B Arbovirus)	Japanese encephalitis, Nakayama			3 (E)		BMBL
Flavivirus	Flaviviruses (others known to be pathogenic)					BMBL
Hepadnaviridae	Hepatitis B virus	*		2		2
Hepadnaviridae	Hepatitis D (Delta) virus (b)	*		2		2
Herpesviridae	Herpesviruses (unassigned, HHV 7, HHV8)	*		2 implied		BMBL
Herpesviridae	Human B lympho-tropic virus					2 (types 6 and 7)
Herpesviridae	Rhadinovirus (except H.ateles,H. saimiri)					
Herpesviridae / Gamma-herpesvirinae	Gammaherpes					
Herpesviridae/ Alphaherpesviridae	Pseudorabies virus					
Herpesviridae/ Alpha-herpesviridae	Herpes simplex viruses	*		2		2 (types 1 and 2)
Herpesviridae/ Alpha-herpesviridae	Herpesvirus simiae (B virus)	*		2/3/4		4
Herpesviridae/ Alpha-herpesviridae	Herpesvirus zoster (Varicella)	*		2		2
Herpesviridae/ Animal virus vector	Herpesvirus saimiri (Genus Rhadinovirus)	*		2 implied		1
Herpesviridae/ Animal virus vector	Marek's disease virus					1
Herpesviridae/ Animal virus vector	Murine cytomegalovirus					1
Herpesviridae/ Animal virus vector	Thetalymphocryptovirus					
Herpesviridae/ Betaherpesviridae	Cytomegalovirus (CMV) (Genus Lymphocryptovirus)			2		2
Herpesviridae/ Gamma-herpesviridae	Epstein-Barr virus (EBV)			2		2

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Table E.3-2. Viral Microorganisms and Their Safety Classifications

Viral Group[1]	Name[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Herpesviridae/ Rhadinovirus	Herpes saimiri	*				1
Herpesviridae/ Rhadinovirus	Herpesvirus ateles	*				1
Herpesviridae/ Rhadinovirus	Rhadinovirus (except H. ateles and H. saimiri)					BMBL
Orthomyxoviridae	Influenza virus (Types A-C)	*		2 (I)		2
Orthomyxoviridae	Influenza virus (vaccine strain)	*		1		BMBL
Orthomyxoviridae	Orthomyxoviridae (Tick-borne encephalitis virus)		*	4	C	BMBL
Orthopoxvirus	Ectromelia (mousepox)					
Papovaviridae	Papillomaviruses (human)					2
Papovaviridae	Polyomavirus (BK and JC viruses)					1
Papovaviridae/ Animal virus vector	Simian virus 40 (SV40)					1
Papovavirus/ Animal virus vector	Shope papilloma virus					1
Papovavirus/Animal virus vector	Bovine papilloma virus					1
Paramyxoviridae	Subsclerosing pancencephalitis					
Paramyxoviridae/ Morbillivirus	Hendra and Hendra-like viruses			3+/4 (I/E)		4
Paramyxoviridae/ Morbillivirus	Measles virus					2
Paramyxoviridae/ Morbillivirus	Morbillivirus (except Rinderpest)					
Paramyxoviridae/ Paramyxovirus	Mumps virus					2
Paramyxoviridae/ Paramyxovirus	Newcastle Disease virus					2
Paramyxoviridae/ Paramyxovirus	Parainfluenza virus (Type 3, SF4 strain)					
Paramyxoviridae/ Paramyxovirus	Parainfluenza viruses					2 (Types 1-4)
Paramyxoviridae/ Pneumovirus	Respiratory syncytial virus					2
Paramyxoviruses/ Parainfluenza viruses	Sendai virus (murine parainfluenza virus type 1)					
Parvoviridae	Parvovirus (human)					2 (B19)
Picornaviridae	Acute haemorrhagic conjunctivitis virus (AHC)					
Picornaviridae	Aphthovirus					
Picornaviridae	Cardiovirus					
Picornaviridae/ Rhinoviruses	Rhinovirus					2
Picornoviridae/ Enterovirus	Coxsackie					2 (Types A and B)
Picornoviridae/ Enterovirus	Echoviruses					2
Picornoviridae/ Enterovirus	Entero					
Picornoviridae/ Enterovirus	Polioviruses	*		2/3		2
Picornoviridae/ Hepatovirus	Hepatitis A virus (human enterovirus type 72)	*		2		2

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Table E.3-2. Viral Microorganisms and Their Safety Classifications

Viral Group[1]	Name[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Poxviridae	Alastrim			2 implied (E)		R
Poxviridae	Buffalopox virus: 2 viruses (1a vaccinia variant)			2 implied (E)		2
Poxviridae	Camel pox virus			2 implied (E)		2
Poxviridae	Cowpox virus			2 (E)		2
Poxviridae	Elephantpox virus (variant of cowpox)			2 (E)		2
Poxviridae	Milker's node virus			2 implied (E)		2
Poxviridae	Molluscum contagiosum virus			2 implied (E)		2
Poxviridae	Paravaccinia virus			2 implied (E)		2
Poxviridae	Rabbitpox virus (vaccinia variant)			2 (E)		2
Poxviridae	Tanapox			2 (E)		2
Poxviridae	Variola (major and minor) virus		✸	R	A	R
Poxviridae	Whitepox (Variola)			R	A	R
Poxviridae	Yabapox virus (Tana and Yaba)			2 (E)		
Poxviridae/ Orthopoxvirus	Monkeypox virus			2 (E)		3
Poxviridae/ Orthopoxvirus	Orthopoxviruses (other pathogenic, not in RG 2 or 4)			2 implied (E)		2
Poxviridae/ Orthopoxvirus	Vaccinia virus			2 (E)		2
Poxviridae/ Parapoxvirus	Orf virus			2 implied		2
Reoviridae	Coltiviruses					2 (incl. Colorado Tick Fever)
Reoviridae	Orbiviruses					2
Reoviridae	Reoviruses					2
Reoviridae	Rotavirus (human)					2
Retroviridae	Lentivirinae (except HIV-1 and HI)	✸		2/3* implied		
Retroviridae	Simian sarcoma virus (SSV-1)			2/3* implied		
Retroviridae/ Lentiviridae	Human Immunodeficiency virus (HIV Types 1 and 2, Oncornavirus C)	✸		2/3*		3 (Types 1 and 2)
Retroviridae/ Lentiviridae	Simian immunodeficiency virus			2/3*		3
Retroviridae/ Oncovirinae	Oncornavirus B			2/3* implied		
Retroviridae/ Oncovirinae	Oncornavirus C (except HTLV I and II)			2/3* implied		
Retroviridae/ Oncovirinae/ Genus Oncornavirus C	Human T-cell lymphotropic viruses (HTLV)			2/3* implied		3 (Types 1 and 2)
Rhabdoviridae	Flanders-Hart Park virus (see Zinsser, pg 777)			2		BMBL
Rhabdoviridae	Hart Park virus (see Zinsser, pg 777)			2		BMBL
Rhabdoviridae	Vesicular stomatitis virus	✸		2/3 (I/E) some R		2 (lab adapted strains), 3
Rhabdoviridae/ Lyssavirus	Rabies virus			2 /3*		2

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Togaviridae/ Alphavirus (Grp A Arbovirus)	Alphaviruses (others known)					
Togaviridae/ Alphavirus (Grp A Arbovirus)	Barmah Forest			2		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	Bebaru virus			2		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	Chikungunya virus			V2 (E), 3 (E)		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	Eastern equine encephalomyelitis (EEE)		✸	2 (I)	B	2
Togaviridae/ Alphavirus (Grp A Arbovirus)	Everglade virus			3		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	Mayaro virus			3		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	Mucambo virus			3		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	Ndumu			3		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	O'Nyong-Nyong virus			2		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	Ross River virus			2		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	Semliki Forest virus			3		3
Togaviridae/ Alphavirus (Grp A Arbovirus)	Sindbis virus			2		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	Tonate virus			3/4 (E), some R		BMBL
Togaviridae/ Alphavirus (Grp A Arbovirus)	Venezuelan equine encephalomyelitis			V2 (E), 3 (I/E)	B	V2, 3
Togaviridae/ Alphavirus (Grp A Arbovirus)	Western equine encephalomyelitis			2 (I)	B	2
Togaviridae/ Pestivirus (Canada)	Hepatitis C	✸		2		2
Togaviridae/ Rubivirus	Rubivirus (Rubella)					2
Toroviridae	Toroviridae					
Unclassified viruses	Hepatitis (bloodborne viruses not yet identified)	✸		2 implied		2 implied
Unconventional agents, prions	Bovine spongiform encephalopathy (BSE)			2* (I)		
Unconventional agents, prions	Chronic wasting disease (CWD)			2		
Unconventional agents, prions	Creutzfeldt-Jacob disese			3		3
Unconventional agents, prions	Exotic ungulate encephalopathy (EUE)			2		

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Table E.3-2. Viral Microorganisms and Their Safety Classifications

Viral Group[1]	Name[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
Unconventional agents, prions	Feline spongiform encephalopathy (FSE)			2		
Unconventional agents, prions	Gatal familial insomnia (FFI)			3		
Unconventional agents, prions	Gerstmann-Straussler-Scheinker syndrome			3*		3 implied
Unconventional agents, prions	Kuru			3*		3
Unconventional agents, prions	Scrapie			2* implied		
Unconventional agents, prions	Transmissible mink encephalopathy (TME)			2		
Viral vector/Animal retrovirus	Avian leukosis virus (ALV)					1
Viral vector/Animal retrovirus	Avian sarcoma virus					1
Viral vector/Animal retrovirus	Bovine immunodeficiency virus (BIV)					
Viral vector/Animal retrovirus	Bovine leukemia virus (BLV)					1
Viral vector/Animal retrovirus	Feline leukemia virus (FeLV)					1
Viral vector/Animal retrovirus	Feline sarcoma virus (FeSV)					1
Viral vector/Animal retrovirus	Gibbon leukemia virus (GaLV)					1
Viral vector/Animal retrovirus	Mason-Pfizer monkey virus					1
Viral vector/Animal retrovirus	Mouse mammary tumor virus					1
Viral vector/Animal retrovirus	Murine leukemia virus					1
Viral vector/Animal retrovirus	Murine sarcoma virus					1
Viral vector/Animal retrovirus	Rat leukemia virus					1
Viral vector/Animal virus	Baculovirus					
Viral vector/Animal virus	Chick embryo lethal orphan (CELO)					
Viral vector/Animal virus	Dog sarcoma					
Viral vector/Animal virus	Guinea pig herpes					
Viral vector/Animal virus	Hamster leukemia					
Viral vector/Animal virus	Lucke (frog) virus					
X-Arboviruses	Aino			3		BMBL
X-Arboviruses	Akabane			3		BMBL
X-Arboviruses	Araguari			3		BMBL
X-Arboviruses	Batama			2		BMBL
X-Arboviruses	Batken			3		BMBL
X-Arboviruses	Bhanja			3		BMBL
X-Arboviruses	Bimbo			3		BMBL
X-Arboviruses	Bluetongue			2 (E)		BMBL
X-Arboviruses	Bobaya			3		BMBL
X-Arboviruses	Bobia			3		BMBL
X-Arboviruses	Buenaventura			3		BMBL
X-Arboviruses	Cabassou			3		BMBL
X-Arboviruses	Cache valley			2		BMBL
X-Arboviruses	Chim			3		BMBL
X-Arboviruses	Cocal			3		BMBL
X-Arboviruses	Dhori			3		BMBL
X-Arboviruses	Dugbe			3		BMBL

[1] Basic name and viral group list is from ABSA 1998 with some additions.
[2] LANL proposed disease list is from PC 2001b
[3] Select agent list is from 42 CFR 72
[4] Biosafety Level is from CDC 1999 - all organisms shown require import or transfer permit from CDC
[5] Risk Grouping from CDC 2000a
[6] NIH Risk Groups (RG) are from NIH 2001
RG 1 not associated with disease in healthy human adults
RG 2 associated with human disease that is rarely serious and prophylactic intervention ***often*** available
RG 3 associated with human disease that is serious or lethal and prophylactic intervention ***may be*** available
RG 4 associated with human disease that is serious or lethal and prophylactic intervention ***not usually*** available
E -- Requires export permit from CDC and/or Deparment of Commerce or USDA
I -- Requires import permit from CDC and/or Deparment of Commerce or USDA
R -- is for restricted authorization to use either by the CDC or USDA
V -- is for vaccine
* activities with high droplet or aerosol production potential

Table E.3-2. Viral Microorganisms and Their Safety Classifications

Viral Group[1]	Name[1]	Current LANL proposed[2]	Select Agents[3]	CDC Biosafety Level[4]	CDC Risk Group[5]	NIH Risk Group[6]
X-Arboviruses	Ganjam (E permit)					
X-Arboviruses	Garba			3		BMBL
X-Arboviruses	Germiston			3		BMBL
X-Arboviruses	Getah			3		BMBL
X-Arboviruses	Gordil			3		BMBL
X-Arboviruses	Guaratuba			2		BMBL
X-Arboviruses	Ibaraki			3		BMBL
X-Arboviruses	Inhangapi			3		BMBL
X-Arboviruses	Inini			3		BMBL
X-Arboviruses	Israel Turkey Mening.			3		BMBL
X-Arboviruses	Issyk-Kul			3		BMBL
X-Arboviruses	Itaituba			3		BMBL
X-Arboviruses	Kairi			3		BMBL
X-Arboviruses	Khasan			3		BMBL
X-Arboviruses	Koutango			3		BMBL
X-Arboviruses	Kyzylagach			3		BMBL
X-Arboviruses	LaCrosse virus			2		BMBL
X-Arboviruses	Langat virus			2		BMBL
X-Arboviruses	Middelburg			3		BMBL
X-Arboviruses	Nariva, Negishi			3		BMBL
X-Arboviruses	New Minto			3		BMBL
X-Arboviruses	Nodamura			3		BMBL
X-Arboviruses	Northway			3		BMBL
X-Arboviruses	Ouango			3		BMBL
X-Arboviruses	Oubangui			3		BMBL
X-Arboviruses	Paramushir			3		BMBL
X-Arboviruses	Piry			3 (I)		BMBL
X-Arboviruses	Razdan			3		BMBL
X-Arboviruses	Rochambeau			3		BMBL
X-Arboviruses	Sagiyama			3		BMBL
X-Arboviruses	Salanga			3		BMBL
X-Arboviruses	Santa Rosa			3		BMBL
X-Arboviruses	Saumarex Reef			3		BMBL
X-Arboviruses	Sepik			3		BMBL
X-Arboviruses	Slovakia			3		BMBL
X-Arboviruses	Spondweni			3		BMBL
X-Arboviruses	Tamdy			3		BMBL
X-Arboviruses	Telok Forest			3		BMBL
X-Arboviruses	Tlacotalpan			3		BMBL
X-Arboviruses	Tocio					BMBL
X-Arboviruses	Turlock virus			2		BMBL
	Nipah virus				C	
	Hemorrhagic fever agents and viruses undefined					4

[1] Basic name and viral group list is from ABSA 1998 with some additions.
[2] LANL proposed disease list is from PC 2001b
[3] Select agent list is from 42 CFR 72
[4] Biosafety Level is from CDC 1999 - all organisms shown require import or transfer permit from CDC
[5] Risk Grouping from CDC 2000a
[6] NIH Risk Groups (RG) are from NIH 2001
RG 1 not associated with disease in healthy human adults
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Table E.3-3. Fungi and their Safety Classifications

Genus[1]	Species[1]	Select Agents[2]	CDC Biosafety Level[3]	CDC Risk Group[4]	NIH Risk Group[5]
Absidia	*corymbifera*				
Absidia	*ramosa*				
Ajellomyces	*capsulatus*				
Ajellomyces	*dermatitidis*				
Aspergillus	*flavus*				
Aspergillus	*fumigatus*				
Aspergillus	*spp*				
Blastomyces	*dermatitidis*		2		2
Candida	*albicans*				
Candida	*spp*				
Cladosporium	*bantianum*		2		2
Cladosporium	*carrionii*				
Cladosporium	*trichoides*		2		2 (Xylo-hypha)
Cladophialopora	*bantians*		2		
Coccidioides	*immitis*		2, 3 arthro-conidia; cont. soil		3 (soil, sporul. cultures)
Cryptococcus	*neoformans*		2		2
Dactylaria	*gallopava*		2		2 (Ochro-conis)
Dermatophilus	*congolensis*				
Emmonsia	*parva*				
Epidermophyton	*floccosum*		2, implied		2, implied
Epidermophyton	*spp*		2		2
Exophiala	*dermatitidis*		2 (Wan-giella)		2 (Wan-giella)
Filobasidiella	*bacillispora*				
Filobasidiella	*neoformans*				
Fonsecaea	*compacta*				
Fonsecaea	*pedrosoi*		2		2
Geotrichum	*spp*				
Histoplasma	*capsulatum*		3 (capsulatum)		3 (capsulatum and duboisii)
Histoplasma	*farcinimosum*				
Histoplasma	*spp.*				
Loboa	*lobai*				
Madurella	*grisea*				
Madurella	*mycetomatis*				

[1] Basic genus and specie list is from ABSA 1998 with some additions.

[2] Select agent list is from 42 CFR 72

[3] Biosafety Level is from CDC 1999 - all organisms shown require import or transfer permit from CDC

[4] Risk Grouping from CDC 2000a

[5] NIH Risk Groups (RG) are from NIH 2001
RG 1 not associated with disease in healthy human adults
RG 2 associated with human disease that is rarely serious and prophylactic intervention often available
RG 3 associated with human disease that is serious or lethal and prophylactic intervention may be available
RG 4 associated with human disease that is serious or lethal and prophylactic intervention not usually available

Table E.3-3. Fungi and their Safety Classifications

Genus[1]	Species[1]	Select Agents[2]	CDC Biosafety Level[3]	CDC Risk Group[4]	NIH Risk Group[5]
Microsporum	*spp*		2		2
Mucor	*spp*				
Neotestudina	*rosatii*				
Ochroconis	*gallopavum*		2		
Paracoccidioides	*brasiliensis*				2
Penicillium	*marneffei*		2		2
Phialophora	*compacta*				
Phialophora	*pedrosoi*				
Ramichlorisium	*mackenzieim*		2		
Rhinocladiella	*compacta*				
Rhinocladiella	*pedrosoi*				
Rhizopus	*cohnii*				
Rhizopus	*microspous*				
Sporothrix	*schenckii*		2		2
Stachybotrus	*atra*		2		
Trichophyton	*rubrum*		2, implied		2, implied
Trichophyton	*spp*		2		2
Trichosporon	*spp*				
Xylohypha	*bantania*				
Zymonema	*dermatitidis*				

[1] Basic genus and specie list is from ABSA 1998 with some additions.

[2] Select agent list is from 42 CFR 72

[3] Biosafety Level is from CDC 1999 - all organisms shown require import or transfer permit from CDC

[4] Risk Grouping from CDC 2000a

[5] NIH Risk Groups (RG) are from NIH 2001
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RG 4 associated with human disease that is serious or lethal and prophylactic intervention not usually available

Table E.3-4. Parasites and Their Safety Classification

Genus[1]	Species[1]	Group[1]	Select Agents[2]	CDC Biosafety Level[3]	CDC Risk Group[4]	NIH Risk Group[5]
Acanthamoeba	*castellani*	Protozoa		2		
Acanthamoeba	*spp*	Protozoa		2		
Acanthocheilonema	*spp*	Helminth, Nematode				
Ancylostoma	*duodenale*	Helminth, Nematode		2 implied		2
Ancylostoma	*spp*	Helminth, Nematode		2 implied		2
Ancylstoma	*ceylanicum*	Helminth, Nematode		2 implied		2
Angiostrongylus	*cantonensis*	Helminth, Nematode				
Angiostrongylus	*costaricensis*	Helminth, Nematode				
Angiostrongylus	*spp*	Helminth, Nematode				
Ascaris	*lumbricoides*	Helminth, Nematode		2 implied		2
Ascaris	*spp*	Helminth, Nematode		2		2
Ascaris	*suum*	Helminth, Nematode		2 implied		2
Babesia	*divergens*	Protozoa		2 implied		2
Babesia	*microti*	Protozoa		2 implied		2
Babesia	*spp*	Protozoa		2		2
Balamuthia	*spp.*	Protozoa		2		
Balantidium	*coli*	Protozoa				
Balantidium	*spp*	Protozoa				
Brugia	*malayi*	Helminth, Nematode		2 implied		2
Brugia	*pahangi*	Helminth, Nematode		2 implied		2
Brugia	*spp*	Helminth, Nematode		2 implied		2

[1] Basic genus and specie list is from ABSA 1998 with some additions.

[2] Select agent list is from 42 CFR 72

[3] Biosafety Level is from CDC 1999 - all organisms shown require import or transfer permit from CDC

[4] Risk Grouping from CDC 2000a

[5] NIH Risk Groups (RG) are from NIH 2001
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Table E.3-4. Parasites and Their Safety Classification

Genus[1]	Species[1]	Group[1]	Select Agents[2]	CDC Biosafety Level[3]	CDC Risk Group[4]	NIH Risk Group[5]
Brugia	*timori*	Helminth, Nematode				2
Capillaria	*philippinensis*	Helminth, Nematode				
Capillaria	*spp*	Helminth, Nematode				
Clonorchis	*sinensis*	Helminth, Trematode				
Clonorchis	*spp*	Helminth, Trematode				
Clonorchis	*viverrini*	Helminth, Trematode				
Coccidia	*spp*	Protozoa		2		2
Cyclospora	*cayetanensis*					
Cryptosporidium	*parvum*	Protozoa		2 implied		2
Cryptosporidium	*spp*	Protozoa		2		2
Cysticercus	*cellulosae*	Helminth, Cestode larva		2		2
Cysticercus	*spp*	Helminth, Cestode		2		2
Dicrocoelium	*spp*	Helminths, Trematode				
Dipetalonema	*perstans*	Helminth, Nematode				
Dipetalonema	*spp*	Helminth, Nematode				
Dipetalonema	*streptocerca*	Helminth, Nematode				
Diphyllobothrium	*latum*	Helminth, Cestode				
Diphyllobothrium	*spp*	Helminth, Cestode				
Dipylidium	*spp*	Helminth, Cestoda				

[1] Basic genus and specie list is from ABSA 1998 with some additions.

[2] Select agent list is from 42 CFR 72

[3] Biosafety Level is from CDC 1999 - all organisms shown require import or transfer permit from CDC

[4] Risk Grouping from CDC 2000a

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RG 4 associated with human disease that is serious or lethal and prophylactic intervention not usually available

Table E.3-4. Parasites and Their Safety Classification

Genus[1]	Species[1]	Group[1]	Select Agents[2]	CDC Biosafety Level[3]	CDC Risk Group[4]	NIH Risk Group[5]
Dracunculus	*medinensis*	Helminth, Nematode				
Dracunculus	*spp*	Helminth, Nematode				
Echinococcus	*granulosis*	Helminth, Cestode		2 implied		2
Echinococcus	*multilocularis*	Helminth, Cestode		2 implied		2
Echinococcus	*spp*	Helminth, Cestode		2		2
Echinococcus	*vogeli*	Helminth, Cestode		2 implied		2
Entamoeba	*histolytica*	Protozoa		2		2
Enterobius	*spp*	Helminth, Nematode		2		2
Fasciola	*gigantica*	Helminth, Trematode		2 implied		2
Fasciola	*Hepatica*	Helminth, Trematode		2 implied		2
Fasciola	*spp*	Helminth, Trematode		2 (metacercariae)		2
Fasciolopsis	*buski*	Helminth, Trematode				
Fasciolopsis	*spp*	Helminth, Trematode				
Giardia	*lamblia*	Protozoa		2 implied		2
Giardia	*spp*	Protozoa		2		2
Hartmanella	*spp*	Protozoa				
Heterophyes	*spp*	Helminth, Trematode		2		2
Hymenolepis	*diminuta*	Helminth, Cestode				2
Hymenolepis	*nana*	Helminth, Cestode		2		2

[1] Basic genus and specie list is from ABSA 1998 with some additions.

[2] Select agent list is from 42 CFR 72

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Table E.3-4. Parasites and Their Safety Classification

Genus[1]	Species[1]	Group[1]	Select Agents[2]	CDC Biosafety Level[3]	CDC Risk Group[4]	NIH Risk Group[5]
Hymenolepis	*spp*	Helminth, Cestode		2		2
Isospora	*spp*	Protozoa		2 implied, Coccidia		2
Leishmania	*braziliensis*	Protozoa		2 implied		2
Leishmania	*donovani*	Protozoa		2 implied		2
Leishmania	*ethiopica*	Protozoa		2 implied		2
Leishmania	*major*	Protozoa		2 implied		2
Leishmania	*mexicana*	Protozoa		2 implied		2
Leishmania	*peruviania*	Protozoa		2 implied		2
Leishmania	*spp.*	Protozoa		2		2
Leishmania	*tropica*	Protozoa		2 implied		2
Linguatula	*spp*	Arthropod				
Loa	*loa*	Helminth, Nematode		2 implied		2
Loa	*spp*	Helminth, Nematode		2 implied		2
Macracanthorhynchus	*spp*	Acanthocephala				
Mansonella	*ozzardi*	Helminth, Nematode				
Mansonella	*perstans*	Helminth, Nematode				
Microsporidium	*spp.*	Protozoa		2 implied		2
Naegleria	*fowleri*	Protozoa		2		2
Naegleria	*gruberi*	Protozoa		1		1
Naegleria	*spp*	Protozoa		2		1 or 2
Necator	*americanus*	Helminth, Nematode		2		2
Necator	*spp*	Helminth, Nematode		2		2
Onchocerca	*spp*	Helminth, Nematode		2 implied		2
Onchocerca	*volvulus*	Helminth, Nematode		2 implied		2

[1] Basic genus and specie list is from ABSA 1998 with some additions.

[2] Select agent list is from 42 CFR 72

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Table E.3-4. Parasites and Their Safety Classification

Genus[1]	Species[1]	Group[1]	Select Agents[2]	CDC Biosafety Level[3]	CDC Risk Group[4]	NIH Risk Group[5]
Opisthorchis	*felineus*	Helminth, Trematode				
Opisthorchis	*spp*	Helminth, Trematode				
Paragonimus	*spp*	Helminth, Trematode				
Paragonimus	*westermanii*	Helminth, Trematode				
Piroplasma	*spp*	Protozoa				
Plasmodium	*cynomologi*	Protozoa		2		2
Plasmodium	*falciparum*	Protozoa		2 implied		2
Plasmodium	*malariae*	Protozoa		2 implied		2
Plasmodium	*ovale*	PRotozoa		2 implied		2
Plasmodium	*simian parasites*	Protozoa		2 implied		2
Plasmodium	*spp*	Protozoa		2		2
Plasmodium	*vivax*	Protozoa		2 implied		2
Pneumocystis	*carinii*	Protozoa				
Sarcocystis	*spp*	Protozoa		2		2
Sarcocystis	*sui hominis*	Helminth, Cestode larva		2 implied		
Schistosoma	*haematobium*	Helminth, Trematode		2 implied		2
Schistosoma	*intercalatum*	Helminth, Trematode		2 implied		2
Schistosoma	*japonicum*	Helminth, Trematode		2 implied		2
Schistosoma	*mansoni*	Helminth, Trematode		2 implied		2
Schistosoma	*mekongi*	Helminth, Trematode		2 implied		2
Schistosoma	*spp*	Helminth, Trematode		2		2
Strongyloides	*spp*	Helminth, Nematode		2		2

[1] Basic genus and specie list is from ABSA 1998 with some additions.

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Table E.3-4. Parasites and Their Safety Classification

Genus[1]	Species[1]	Group[1]	Select Agents[2]	CDC Biosafety Level[3]	CDC Risk Group[4]	NIH Risk Group[5]
Strongyloides	*stercoralis*	Helminth, Nematode		2 implied		2
Taenia	*saginata*	Helminth, Cestode				
Taenia	*solium*	Helminth, Cestode		2		2
Taenia	*spp*	Helminth, Cestode				2
Toxascaris	*spp*	Helminth, Nematode				
Toxocara	*canis*	Helminth, Nematode				2
Toxocara	*spp*	Helminth, Nematode				2
Toxoplasma	*gondii*	Protozoa		2 implied		2
Toxoplasma	*spp*	Protozoa		2		2
Trichinella	*spiralis*	Helminth, Nematode				2
Trichomonas	*vaginalis*	Protozoa				
Trichostrongylus	*spp*	Helminth, Nematode				
Trichuris	*trichiura*	Helminth, Nematode				
Trypanosoma	*brucei brucei*	Protozoa		2 implied		2
Trypanosoma	*brucei gambiense*	Protozoa		2 implied		2
Trypanosoma	*brucei rhodensiense*	Protozoa		2 implied		2
Trypanosoma	*cruzi*	Protozoa		2 implied		2
Trypanosoma	*spp*	Protozoa		2		2
Wuchereria	*bancroftii*	Helminth, Nematode		2 implied		2
Wuchereria	*spp*	Helminth, Nematode		2		2

[1] Basic genus and specie list is from ABSA 1998 with some additions.

[2] Select agent list is from 42 CFR 72

[3] Biosafety Level is from CDC 1999 - all organisms shown require import or transfer permit from CDC

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